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CARDIAC CHANGES IN PREGNANCY UNRELATED TO THE USUAL ETIOLOGICAL TYPES OF HEART DISEASE

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THE frequency with which symptoms and signs of cardiac failure appear ante partum and post partum in women who had no evidence of heart disease before becoming pregnant is not known. Observation of such patients has prompted the present report. These patients were found by examining women who, at the time they became pregnant, had apparently normal hearts, and by selecting from obstetric cardiac patients those who did not have the usual types of heart disease. The report is necessarily incomplete, for it represents only those patients observed personally. The findings were grouped arbitrarily, as follows: (1) physiologic changes, including so-called "gestatory heart disease"; (2) changes dependent upon toxemia and nephritis; and (3) post-partum heart failure. A preliminary report of some of these observations has already been given,[1] and certain aspects of the post-partum group have been described.[2]

PHYSIOLOGIC CHANGES

Seventy-three apparently normal patients were followed through pregnancy, by the usual clinical methods, to ascertain what cardiac changes resulted from the gravid state. Thirty-one, less than one-half, developed palpitation or dyspnea, or both, of sufficient severity to constitute a complaint. Only two patients suffered from choking or "smothering" at night. Soft systolic murmurs were common and, at times, were markedly affected by posture. In thirty instances, soft, short, transient, systolic pulmonic murmurs were heard. Of the more constant systolic murmurs, eighteen were both apical and basal, six were apical alone, and eight were basal alone. A diastolic murmur, high-pitched and blowing in character, was heard at the aortic area in

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one patient. Gallop rhythm occurred eight times, and a definite accentuation of the pulmonic second sound, thirty-one times. Accentuation of the aortic second sound was found twice, and splitting of the mitral first sound, five times. The heart was definitely beyond the midclavicular line in twelve cases, in ten of which the presence of enlargement was confirmed by roentgenologic examination. Tachycardia was recorded graphically at one time or another in forty-seven cases. Ectopic beats were recorded electrocardiographically in four. No significant electrocardiographic changes developed in the standard leads. In twenty-eight instances there was definite edema of the ankles. The blood pressure remained within the normal range in every case.

Seven of the seventy-three patients developed symptoms and signs which, in the last trimester of pregnancy, were sufficient to suggest heart disease. In five of these, palpitation and dyspnea on exertion were accompanied by accentuation of the pulmonic second sound, extension of the left border of cardiac dullness beyond the midclavicular line, and systolic apical murmurs, and, in two instances, by basal systolic murmurs, edema of the ankles, and coarse râles at the bases of both lungs. In one instance, numerous ventricular extrasystoles occurred, and, in one, sensations of suffocation awakened the patient and caused her to sit up for short periods on several occasions in the eighth month. The sixth patient had dyspnea on exertion, extension of the left border of cardiac dullness 1 cm. to the left of the midclavicular line, a metallic, sharply accentuated aortic second sound, a split mitral first sound, a soft pulmonic systolic murmur, and edema of the ankles. The seventh experienced mild dyspnea on exertion and showed, on physical examination, a high-pitched, blowing, diastolic murmur, heard best in the aortic area and along the left border of the sternum.

In two of the patients, symptoms were very marked. In one, dyspnea became so severe that the patient was unable to carry on her usual household duties. She required frequent rest and complained of fatigability. In the other, the symptoms were similar, but were accompanied by marked apprehension, a coarse tremor of the hands, tachycardia, and evidence of vasomotor instability. In no instance were the neck veins distended, and in three patients indirect measurement of the venous pressure on the dorsum of the hand showed that it was normal. The arterial pressure was within the normal range in all patients. In each instance delivery was uneventful, and examination during the puerperium disclosed that practically all of the signs and symptoms had disappeared.

DISCUSSION

The incidence of organic heart disease in pregnancy varies with many factors, chiefly with the soundness of the criteria used in diag-

nosis, geographic location, and the type of patient studied. Among 100,228 obstetric cases, there were 823 reported instances of organic heart disease, an incidence of 0.82 per cent,[3] or, in general, approximately 1 per cent. Still, reports[4] show that as high as 7.5 per cent of all women admitted to ante-partum clinics have shown something in the history or physical examination to suggest heart disease. Others[5] have found that as many as 50 per cent of all pregnant women who present cardiac signs and symptoms do not have organic heart disease. The discrepancy between 0.82 per cent and the values just given is no doubt caused by a difference in diagnostic criteria, for many of these manifestations, which are usually caused by heart disease, are normal occurrences in the normal pregnant woman and therefore cannot be interpreted as evidence of heart disease. In the group of seven patients with unusually marked symptoms and signs, the findings appeared to be, in general, an exaggeration of those found in the group as a whole.

The incidence of murmurs varies widely, according to the literature. In eighteen reports, Jensen[6] found values from 0.7 per cent to 75.0 per cent, with an average of 28.6 per cent. Many of these figures are probably too low, for the incidence of murmurs varies with the diligence with which they are sought. In the present group, careful search showed that, in thirty-three of seventy-three patients (45.2 per cent), murmurs were constantly present after they were discovered. This value is raised to 86.3 per cent if inconstant pulmonic systolic murmurs are included, but not to 100 per cent, as indicated in a recent report.[7] Most typically, these murmurs were soft and were located in the pulmonic area. Occasionally they were loud, and often the localization was apical and basal. As a rule, the apical murmur was fainter than that in the pulmonic area, and, at times, was heard only with the patient bending forward or in the left lateral position. In one instance the apical murmur was more marked, was accompanied by a definite thrill, and was transmitted to the axilla. Two of the six apical, and three of the basal, murmurs failed to disappear post partum; in these patients the murmurs were present, but less loud, when the patient was first seen in the first trimester. Apparently they were present before pregnancy. In the remaining patients, the murmurs appeared in the second and third trimesters.

Changes in the cardiac tones are frequent in pregnancy. The mitral first sound may become louder or softer, more often the former. In five of the present patients, splitting of the apical first sound was noted. Accentuation of the pulmonic second sound, which is said to occur in from 27 to 50 per cent of pregnant women,[6] was present in 42.5 per cent of the present series. This value would have been higher had less distinct examples been included, and had more definite points of reference been available. It has been ascribed to a number

of factors, including increased pressure in the pulmonary circuit and cardiac rotation which places the heart in a more favorable position for auscultation. Accentuation of the aortic second sound occurred much less frequently. Whether cardiac rotation may account for this unusual change is not known. Other possible causes of changes in the heart tones will be given below.

Gallop rhythm developed eight times (9.1 per cent). It was usually heard best just inside and slightly above the apex and occurred at the time of the physiologic third sound, from which it could not be differentiated. Its possible significance will be discussed below.

Little is known of the effects of pregnancy upon the normal heart, despite the many attempts to solve this problem. The diaphragm is elevated by the growing uterus. Cardiac displacement takes place, with an increase in the cardiac dullness to percussion and an increase in the transverse diameter as measured by teleoroentgenograms. Yet not all of this change is caused by cardiac displacement, for enlargement of the cardiac shadow has been observed before displacement could be held accountable for it.[8] Likewise, physiologic, as well as anatomic, changes occur. Metabolic processes are accelerated. New endocrine relationships appear. The enlarging uterus and its contents require nourishment and increase circulatory demands.

Reliable methods[9, 10] indicate that cardiac output is increased in pregnancy to as much as 50 per cent above normal in the latter half. Stander and Cadden[10] point out that, since normal pregnancy is not attended with an appreciable drop in blood pressure, normal gestation is accompanied by a marked increase in cardiac work. Other physiologic studies[7, 11] are in accord with this. Oxygen consumption, velocity of blood flow, and blood volume are increased. These changes increase progressively until the last month of pregnancy, when a return toward normal begins. All evidence, from the increased frequency of heart failure in organic heart disease as pregnancy progresses, to special studies of the circulatory constants, points to an increased strain upon the heart.

A possible explanation for the development of these changes has been advanced by Burwell and his associates.[11, 12] They point out that patients with arteriovenous fistula have tachycardia, an increased pulse pressure (at times with peripheral signs comparable to those produced by aortic regurgitation), an increase in cardiac output per minute, a decrease in arteriovenous oxygen difference, an elevated pressure in the veins adjacent to the fistula, a higher oxygen saturation of the blood in these veins than in mixed venous blood, an increase in total blood volume, a murmur in the region of the fistula, and dilatation of the artery leading to the fistula. These phenomena include those described above as occurring in pregnancy, and the remainder, except the last, have been shown to be present in pregnant women,

although not to the marked degree often seen in cases of arteriovenous fistula. Burwell believes that the changes in pregnancy result, in the main, from a similar mechanism, i.e., an arteriovenous communication in the placenta, and from obstruction to venous return by the enlarged uterus. Others[7] suggest that such a mechanism does not appear to account for all of the changes which occur. Furthermore, they are unable to correlate this explanation with the fact that there is a return toward normal of some circulatory functions before delivery.

The increased work of the heart, together with the apparent increase in its size, suggests that pregnancy alone may produce cardiac hypertrophy. Here, again, opinion is divided, and the results of separate investigations are not in agreement.[13-16] Studies on experimental animals have shown no change in the actual size of the heart during pregnancy, and similar studies in women have been negative. Yet increased cardiac work may produce hypertrophy which is not grossly apparent, and all of the factors mentioned add a cardiac strain which is responsible, in part at least, for changes in sounds, gallop rhythm, murmurs, tachycardia, palpitation, and dyspnea. Mere anatomic readjustments may be responsible, in part, for changes in the pulmonary second sound and edema of the ankles; the latter is caused partly by interference with the return of blood from the lower extremities due to pressure from the enlarging uterus. Thus, increased work and pressure phenomena appear to account for the usual cardiac changes in normal pregnant women, but unequivocal explanations cannot be given for most of these changes.

As a rule, the symptoms and signs which developed in women who showed no evidence of heart disease before becoming pregnant gave no difficulty in diagnosis. This was true in sixty-six of the seventy-three patients followed. The remaining seven displayed marked symptoms which, together with the objective manifestations, led to difficulties in diagnosis, and this aspect appears to differentiate the two groups. When the physical signs were marked and occurred in a patient who was having pronounced subjective symptoms and obvious dyspnea on exertion which was out of proportion to that usually seen in pregnant women, it was difficult, if not impossible, to rule out the possibility of organic heart disease at that time. The clinical manifestations were readily and clearly recognized when seen from the first stages of their development.

One patient showed distinct indications of neurocirculatory asthenia. Whereas in all of them there were no symptoms at rest, and dyspnea, palpitation, and fatigability developed only on exertion, in only one was there pronounced consciousness of the heartbeat, together with dizziness, vasomotor phenomena, with cold, clammy hands, an anxious expression, and a coarse tremor. In nonpregnant patients this

syndrome is likely to be taken to indicate organic heart disease, and even then a period of observation may be necessary to evaluate symptoms and make the diagnosis. Obviously, this problem, concerning which, in pregnancy, little has been written, becomes more difficult in the presence of the cardiac changes of pregnancy.

One of the remaining patients displayed a blowing, basal, diastolic murmur. Diastolic murmurs have been observed in pregnancy, in the absence of the usual causes of these murmurs, for many years. They disappear in the puerperium. Such murmurs are usually basal and interfere little with the diagnosis of mitral stenosis. They are, however, exceptions to the usual rule that diastolic murmurs are organic in nature, and, together with an increase in the size of the heart, can add considerable confusion to diagnosis.

All seven of these patients followed the same course. All passed through pregnancy and the puerperium without complications. Attempts to alleviate the symptoms, except by rest, were of no avail. Digitalis, as would be expected, had no effect.

This syndrome has been called gestatory heart disease, or, in European writings,[8, 14] functional heart disease of pregnancy. Etiologically, the advisability of such a designation is doubtful, but clinically the term is useful. It has been considered as a possible result of relative insufficiency of the tricuspid valve and of hypertrophy produced by the strain of normal pregnancy. The controversy concerning cardiac hypertrophy in normal pregnancy has already been mentioned and will not be reopened here. Increased cardiac work as a result of the increased demands of pregnancy, changes in the position of the heart, and the effect of the placenta, acting as an arteriovenous fistula, singly or in combination, may be important in the production of this syndrome. The exact mechanism is not known.

The most important thing is to recognize gestatory heart "disease" for what it actually is. As stated above, this problem becomes a difficult one only rarely, and then chiefly when the patient is examined for the first time in the last trimester of pregnancy. Had the patients described here been seen for the first time in the eighth month, the cardiac enlargement, murmurs, and changes in the heart sounds, in view of the symptoms and edema, would have been difficult to interpret. There could have been no assurance that such things as murmurs and cardiac enlargement were not present before pregnancy, and in the evaluation of these findings lies the interpretation of the symptoms of early congestive heart failure. It has been suggested[8, 14] that patients of this type have been included in statistical studies of organic heart disease in pregnancy, and this is very likely true.

Except for cardiac enlargement, and, rarely, the basal diastolic murmur, the signs of heart disease which are pathognomonic when a woman is not pregnant retain their value in the gravid state, and

if they are not present during the childbearing period, there is usually no organic heart disease.[17] Notable exceptions are the occurrence of acute rheumatic fever and bacterial endocarditis. In pregnancy both of these are rare.

The frequency of gestatory heart "disease" in the present group (9.5 per cent) emphasizes its importance from the standpoint of diagnosis. The incidence was still higher in Jensen and Norgaard's[8] series of 239 cases (16 per cent). The syndrome is more common than organic heart disease, and the problem of differential diagnosis becomes apparent. Danger may accompany delay until the full picture of failure develops in cases of organic heart disease, and such manifestations as tachycardia, persistent cough, or increasing dyspnea demand not only the closest supervision, but active therapeutic measures as well.[6] These early signs and symptoms also occur in gestatory heart "disease," but the grave prognosis in the cases of organic heart disease, particularly if based on an estimation of functional capacity, does not apply to this group.

The differentiation of so-called gestatory heart disease from organic heart disease is most important from the standpoint of therapy. These patients require no special treatment, such as rest or drugs, or any deviation from the usual obstetric procedures which are followed when there are no cardiac symptoms. The pregnant woman with organic heart disease, however, requires, if there is evidence of early congestive failure, a highly restricted existence, rest in bed, digitalis therapy, careful observation, and possibly some unusual mode of delivery, such as cesarean section. The inclusion of patients with gestatory heart "disease" in the organic group not only causes them unnecessary expense, inconvenience, and worry, but exposes them unnecessarily to added obstetric risks.

CARDIAC CHANGES ASSOCIATED WITH THE TOXEMIAS OF PREGNANCY

CASE 1.—A housewife, 24 years old, reached the eighth month of her third pregnancy without complaint. Both previous pregnancies had been normal. The blood pressure rose gradually to 140/96, and slight albuminuria developed. At that time the blood pressure rose suddenly to 180/100, and headache and dizziness developed. Paroxysmal nocturnal dyspnea made its appearance. The aortic second sound, which had become accentuated, was exceeded in intensity by the pulmonic second sound. Dyspnea on exertion, râles at the bases of the lungs, and evening edema appeared. Rest in bed and digitalization caused a recession of the symptoms of congestive failure, but the blood pressure remained elevated. The patient entered labor and was delivered without complication. All symptoms and abnormal signs disappeared post partum.

Other patients, similar to the above in certain respects, have been seen from time to time. In cases of so-called pre-eclampsia, with albuminuria and elevated blood pressure but no subjective symptoms, the cardiac manifestations have usually been only those which occur in normal pregnancy. In patients with a pre-existing chronic nephritis and hypertension, the added burden of exacerbation of the disease and of pregnancy has precipitated a low-grade congestive heart failure.

Careful examination of such patients is necessary for early recognition of the signs of left ventricular failure. When the patient has had acute nephritis, the cardiac manifestations, in cases in which they have developed, have been those of acute left ventricular strain, including accentuation of the pulmonic second sound, cardiac dilatation, gallop rhythm, tachycardia, and electrocardiographic changes in the voltage of QRS and in T_1 and T_2.

Discussion.—When one searches the literature for information concerning congestive heart failure complicating the toxemias of pregnancy, one readily finds reference to mitral stenosis and toxemia resulting in congestive heart failure, but little else. Case reports of congestive heart failure in association with toxemia are not difficult to find,[18] but this complication is given little or no consideration in articles[19] and texts.[20]

That congestive heart failure may be expected in the absence of rheumatic heart disease in toxemic patients is evident from the heterogeneous nature of the conditions included under this term. Aside from "true" hypertensive toxemia, this term includes those instances of hemorrhagic nephritis, essential hypertension, malignant hypertension, and pyelonephritis which occur with, or become apparent during, pregnancy. As Zimmerman and Peters[18] have said, "A great variety of vascular or renal diseases may act as predisposing causes for toxemias; pregnancy appears to give them a distinctive coloration and an explosive character." If such a disease antedates pregnancy, it may have encroached to some extent upon the cardiac reserve. Then, with the additional burden of pregnancy and of the added hypertensive disease, either of which alone frequently precipitates heart failure in patients whose hearts are already embarrassed, congestive failure may occur. One would expect the cardiac changes which accompany the toxemic states to vary with their etiology, and this has been our experience.

The "explosive character" which pregnancy seems to confer upon hypertensive disease is obscure etiologically. The results of recent work on animals, however, may have some bearing on the nature of this factor. Dill and Erickson[21] found that dogs which had been made hypertensive by the Goldblatt method showed a marked exacerbation of the process when they became pregnant. Whereas the control animals showed only slight lesions, the pregnant animals developed widespread hepatic lesions similar to those of eclampsia, hemorrhage, and infarction of the myocardium, and evidence of terminal, acute, cardiac failure and pulmonary edema. Such observations suggest that in the pregnant woman with nephritis the marked cardiovascular symptoms and signs may have a similar origin. We have found that the hypertensive symptoms in such patients are explosive in character, not only before delivery, but during the puerperium, as well.

A discussion of nephritis as a cause of cardiac failure will be postponed until post-partum nephritis has been considered.

The presence of added factors which are known to lead to cardiac strain, such as the toxemic syndromes, necessitates close and frequent scrutiny of the patient for early evidences of cardiac insufficiency, which is likely to be masked by the ever-present cardiac changes of normal pregnancy.

POST-PARTUM HEART FAILURE

The occurrence of heart failure post partum, when the heart has been adequate throughout the pregnancy, has not been unusual in the Medical Wards of the Charity Hospital. The patients fall definitely into two groups which are best illustrated by short case summaries. Case 3 has been reported[2] previously as Case 5 in the earlier article.

CASE 2.—A negress, 24 years old, was admitted to the medical service complaining of shortness of breath and "swelling." Three weeks previously she had been delivered, without instrumentation, of her first child. There had been no complications, and she was up and about on the tenth day post partum. Eight days later she was awakened by shortness of breath. The next day swelling of the ankles started, and this progressed until marked edema was present. During the antepartum and lying-in periods, the blood pressure and urine were normal, and physical examination was negative. Examination on admission disclosed a blood pressure of 144/100, enlargement of the heart beyond the left midclavicular line, accentuation of the pulmonic second sound, tachycardia, and a protodiastolic gallop rhythm which was heard best inside the apex. Râles were present at the bases of the lungs, and peripheral edema was marked. An electrocardiogram showed low voltage in all leads and inversion of T_1, with flattening of T_2. The patient was put to bed and given digitalis and diuretics, and in three weeks she had recovered.

CASE 3.—A 25-year-old negress entered the hospital in labor and was delivered of a full-term child by means of forceps. There was no evidence of renal disease at that time. The blood pressure was not elevated. On the fourth and fifth days post partum, the body temperature rose to 101° F., but otherwise the lying-in period was uneventful. About sixteen days post partum she experienced a severe headache, and her vision became blurred at times. She felt feverish, but did not take her temperature. Edema made its appearance about the face and ankles, generalized twitchings developed, and she was readmitted to the hospital. The past history was not contributory. Examination disclosed generalized edema, especially over the eyelids, a blood pressure of 156/100, a temperature of 98° F., and a pulse rate of 90 per minute. The tonsils were not inflamed. There were fine râles at the bases of the lungs. The heart was not demonstrably enlarged to the left. An apical systolic murmur was heard; the pulmonic second sound was louder than the aortic second. There was no evidence of ascites. The urine contained albumin, and many erythrocytes, leucocytes, and coarse granular casts. The nonprotein nitrogen content of the blood was 30 mg. per cent, the sugar content, 97 mg. per cent, and the blood Wassermann reaction was weakly positive.

The patient became progressively worse. The dyspnea grew more marked, and pronounced pulmonary edema developed. The blood pressure remained in the range of 168 to 152, systolic, and 115 to 92, diastolic. The pulse became thready, and the patient died of acute heart failure. No autopsy was done.

Discussion.—These patients are typical of a group seen in the Colored Female Medical Service of the Charity Hospital. Those similar to the patient in Case 2 have shown, previous to delivery, little or no evidence of cardiac failure, but from fourteen to twenty-five days post partum they have developed typical congestive heart failure. Usually in the ante-partum period there have been no evidences of hypertension or other possible causes of heart disease, and usually there has been no evidence of heart failure in that period. Yet, from fourteen to twenty-five days post partum, left-sided, then right-sided, heart failure has made its appearance. At a time when the usual patient with heart failure complicating pregnancy is improving, those in the present group are developing the active phases of the disease. The manifestations are quite typical. Sudden dyspnea, cardiac dilatation, accentuation of the pulmonic second sound, gallop rhythm, pulmonary congestion, marked peripheral edema, elevation of the diastolic pressure without a comparable rise in systolic pressure, and electrocardiographic changes are characteristic. Recovery is slow. Rest in bed is essential. Digitalis and the other therapeutic agents which are usually effective in heart failure have been of doubtful benefit.

In our experience the outcome in these cases has usually been good. We have seen no deaths. Others[23] have reported post-mortem observations on similar patients with serious vascular complications and have described myocardial degeneration different from that produced by the usual etiologic types of heart disease. Focal lesions, with cellular infiltration leading to fibrosis and scar formation, were described. Again, such observations suggest that a factor peculiar to pregnancy may be important in these cases.

This syndrome, although not peculiar to the puerperium, is most characteristic and indicates that the danger of heart failure, although infrequent in the puerperium, may extend beyond the usual lying-in period, to appear suddenly when least expected.

Diastolic hypertension is almost invariably present and appears to be, along with the agent producing it, of etiologic importance. Many etiologic possibilities have been considered, but none has been satisfactorily related to the clinical manifestations. Possible relationships to pregnancy and the puerperium are not understood. Parity and obstetric complications do not appear to be of primary importance. Changes in endocrine functions may be a factor. The fact that the pituitary gland is involved both in pregnancy and certain hypertensive states is well known, and all patients experience some rise in blood pressure at the onset of lactation.[22] Other changes may be contributory. Nutritional deficiency is common in the patients who display this picture. Lastly, one must remember that the time at which symptoms arise coincides with the period at which these patients resume full exercise and place an additional strain upon their hearts.

Case 3 typifies the second group. This patient, unlike the one in Case 2, manifested all the criteria that were necessary for the diagnosis of acute diffuse hemorrhagic nephritis, so that these post-partum syndromes may be divided into at least two groups—a nephritic and a nonnephritic one. This grouping has been confirmed by Addis counts upon the urine.[2]

These two groups have many aspects in common. Both syndromes have occurred in patients who had been followed prenatally, with histories, physical examinations, repeated blood pressure measurements, and urinalyses, none of which disclosed any evidence of vascular or renal disease ante partum. In both groups there is a latent period of from two to three weeks between delivery and the development of symptoms. The symptomatology and cardiac manifestations have been quite similar in the two groups, namely, sudden dyspnea, cardiac dilatation, accentuation of the pulmonic second sound, gallop rhythm, and electrocardiographic changes. At times, as in Case 3, pulmonary congestion has occurred in the nephritic group. The presence of edema in both groups again demonstrates their similarity. However, in the nephritic group, although we have found evidence of acute left ventricular failure, evidence of right-sided heart failure has been lacking, and the edema has been interpreted as nephritic in origin.

Certain differences in these patients are also outstanding. In the nephritic group there has usually been, as in Case 3, some evidence of sepsis in the first few days of the puerperium, often initiated by a distinct chill. Following the evidence of sepsis, a latent period of from fourteen to twenty-one days is followed by evidences of hemorrhagic nephritis, including significant hematuria, albuminuria, casts in the urine, and edema, in addition to vascular changes.

Diastolic hypertension in the nephritic group has been as striking and marked as in the nonnephritic group, and often has been accompanied by symptoms of encephalopathy. The explosive character of the hypertension in this group deserves the same consideration as has already been mentioned in connection with the nonnephritic group.

Heart failure in acute nephritis is in no way peculiar to the post-partum period.[24, 25] Master, Jaffé, and Dack[24] have emphasized the frequency of dyspnea, orthopnea, and pulmonary edema, even, at times, with minimal urinary abnormalities. In their patients, as in our puerperal group, hypertension has been constant and outstanding, with evidence of left ventricular, and absence of right ventricular, failure.

Post-partum nephritis has been rarely recognized.[2] The relationship of its development to the signs of sepsis in the first few days of the puerperium, and the relationship, in turn, of these occurrences to delivery are not settled. At times, bacteriologic studies have shown a streptococcus, but what part this organism may play is as uncertain

in these patients as in patients who have not been pregnant. Nephritis has followed the post-partum fever in from twelve to twenty-one days, a period usually observed in the development of nephritis in general. Age, parity, and the type of delivery have appeared to have little to do with the disease.

SUMMARY AND CONCLUSIONS

Cardiac abnormalities have been pointed out in patients who had apparently normal hearts before they became pregnant. These patients have been divided into 3 groups, as follows:

1. Physiologic changes vary widely, and at times they become sufficiently marked to cause difficulty in diagnosis. It is important to recognize this syndrome, which has been called gestatory heart disease, in order to prevent unnecessary obstetric procedures and to avoid needless restrictions on the activity of such patients in the last trimester.

2. In the course of hypertensive toxemias of pregnancy and acute hemorrhagic nephritis in the ante-partum period, cardiac failure, which may be acute or chronic, left-sided or right-sided, may develop. The manifestations depend primarily upon the underlying pathologic state and vary as widely as do those in the heterogeneous group of conditions included under the term "hypertensive toxemia."

3. Cardiac failure may develop from two to four weeks post partum in patients who have shown little or no evidence of heart failure ante partum. Although the etiology in this group remains obscure, at least two types, a nephritic and a nonnephritic, have been recognized. Their course and outcome have been described.

In each of these three groups, possible etiologic factors and mechanisms of development have been discussed, and diagnostic and therapeutic aspects have been pointed out.

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THE RELATION OF LONGITUDINAL TENSION OF AN ARTERY TO THE PREANACROTIC (BREAKER) PHENOMENON

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IN 1916, the hypothesis was advanced that the arterial sounds of Korotkoff are caused by water hammer.[1] This hypothesis was suggested by a number of observations, but particularly by the fact that, while a compressed artery is emitting the snapping sounds, the front of the arterial pulse recorded just *beyond* the compression chamber is (1) steeper and (2) higher than at other times, and that (3) "the sound waves occupy the very beginning of the peripheral pulse." It seemed that both these phenomena and the snapping sounds could be the result of an impact struck by a column of blood moving through the compressed artery, as it is opened by the pulse, against the stationary column of blood in the uncompressed artery beyond the compression chamber. Observations made a few years later[2, 3, 4] on the movements of the arterial wall *within* the compression chamber, and on the movements in a model, the construction of which was suggested by the animal experiments, brought to light evidence which was incompatible with the water hammer hypothesis; the snapping sounds then were ascribed to the "preanacrotic phenomenon," a phenomenon that develops as the wave travels along a flexible, elastic tube, such as an artery or the inner tube of a bicycle tire, filled, but not stretched annularly, by liquid, which is the state in which the artery finds itself while the snapping sounds are in evidence during decompression. In 1925, Bramwell[5] showed that the phenomenon which had been named "preanacrotic," without commitment as to its mechanism, is the result of the breaking of the propagated wave.

In 1931, Frank and Wezler,[6] unaware of any of the foregoing studies, redescribed the preanacrotic phenomenon in every detail. In addition, they reached the conclusion, on the basis of experiments on excised arteries, that the phenomenon develops only when the artery is stretched longitudinally. Although the arterial model previously employed by us had not been stretched longitudinally and yet had exhibited the phenomenon, it nevertheless seemed desirable, under the circumstances, to ascertain what might be the effect of such stretching on the preanacrotic phenomenon.

The preanacrotic phenomenon can be regarded as being operative when the wave travels some distance along the "artery" before it develops its maximum lateral impact. To determine conveniently

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whether the phenomenon is in evidence, and, if so, where the impact becomes maximum, certain changes were made in the apparatus previously used. Uniform levers, spaced about 6 cm. apart, were arranged along the length of the horizontally placed "artery" so that they crossed it horizontally and were tangent to its upper apex. A solenoid hammer generated pulses at one end of the "artery." By grading the current through the solenoid, the strength of the pulse could be nicely controlled. The amount of current was determined that just sufficed to throw one lever, or two adjacent levers when the effect was the same on two, from the artery under the various imposed conditions (Table I). These included (1) stretching the "artery" longitudinally with weights of 0.2, 0.8, and 1.4 kg. (0.2 kg. was the lightest practicable weight that could be employed) and (2) varying the water pressure in the "artery." The pressures used were short of those that distended the "artery," since it is known[4, 5] that the fuller the "artery," the further must the wave travel before the preanacrotic phenomenon develops, and that in the distended rubber tube the phenomenon develops only after the wave has traveled an infinite distance—that is to say, it does not develop at all. Therefore, in the present experiments the distending pressure was kept meticulously at the same level in each set of determinations of the effect of the three different extensions employed.

TABLE I*

STRETCHING WEIGHT (KG.)	LENGTH OF "ARTERY" (CM.)	PRESSURE (CM. H_2O)	RELATIVE PULSE VELOCITY	CURRENT NEEDED TO THROW LEVER (AMP.)	LEVER THROWN	
					NO.	DISTANCE FOR MAXIMUM IMPACT (CM.)
0.2	105	3.55	90	2.62	4	21.6
0.8	111	3.55	94	2.78	4–5	24.4
1.4	120	3.55	97	2.97	5	27.2
0.2	105	5.1	105	2.52	6-	34.0-
0.8	111	5.1	111	2.73	6	34.0
1.4	120	5.1	115	2.90	6	34.0
0.2	105	6.7	109	2.71	6+	34.0+
0.8	111	6.7	116	2.87	6–7	37.1
1.4	120	6.7	122	3.30	6	34.0

*The determinations are grouped under the three different "arterial" pressures used, namely, 3.55, 5.10, and 6.70 cm. H_2O, and in each group they are arranged in the order of the stretching weights applied.

A set of these observations is collected in Table I. It is seen that, whether the tube is extended or not, the phenomenon is in evidence; depending upon the degree of fullness of the "artery" within the limits mentioned, the wave travels from 22 to 37 cm. before it develops a maximum impact. It is clear, moreover, that the greater the extension of the tube, the stronger must the pulse stroke be to throw a lever from the artery. And, finally, it is seen that, at the lesser degrees of distention, the greater the extension, the further must the wave travel in order to develop its maximum impact. In other words, longitudinal

stretching is not only unnecessary for the development of the phenomenon, but actually hampers its development, as might have been predicted from what is known regarding breaker formation in elastic tubes.

How then are the results of Frank and Wezler to be accounted for? We are convinced that they are attributable to an error in technique. In their experiments, the artery was not exposed to compression from without; instead, it was compressed by reducing the internal pressure (i.e., by suction), and pulses were produced by opening a stopcock on a tube connecting the artery with a pressure bottle. Now, under these circumstances, the slightest negative inside pressure would collapse the artery when it was unextended. But, tied as it was to terminal cannulae, the artery would resist a pressure differential tending to cause it to collapse, and this would be in direct proportion to any longitudinal pull exerted on it through the medium of the cannulae. With the arrangement employed, the artery would remain collapsed until the longitudinal pull became sufficient to counterbalance the internal negative pressure. It was not the longitudinal stretching, per se, that permitted the negative wave of the preanacrotic phenomenon to develop, but the presence of the diastolic residuum[4] determined by the longitudinal tension, without which there could be no preanacrotic negative wave.

Previous experiments have shown[4] that the intensity of the sound that develops at the point of maximum impact diminishes as the "artery" approaches distention. The present experiments show that longitudinal extension of the artery has the same effect on the emitted sounds as distention.

CONCLUSION

Longitudinal tension is not a necessary condition for the development of the preanacrotic (breaker) phenomenon during the propagation of a wave along elastic tubes; on the contrary, such stretching increases the distance the wave must travel in order to break, and it diminishes the intensity of the associated sound.

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ROENTGENOLOGIC DEMONSTRATION OF LEFT VENTRICULAR HYPERTROPHY

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THE purpose of this paper is to evaluate measurement of the thickness of the left ventricle by means of roentgenologic examination. The method first described by Vaquez[1] has been found useful in our studies.

A line is drawn from the left auriculoventricular sulcus to the apex. A perpendicular erected on this line from the point of greatest salience of the left ventricular contour ("bisector") is an approximate measure of the thickness of the left ventricle (Fig. 1).

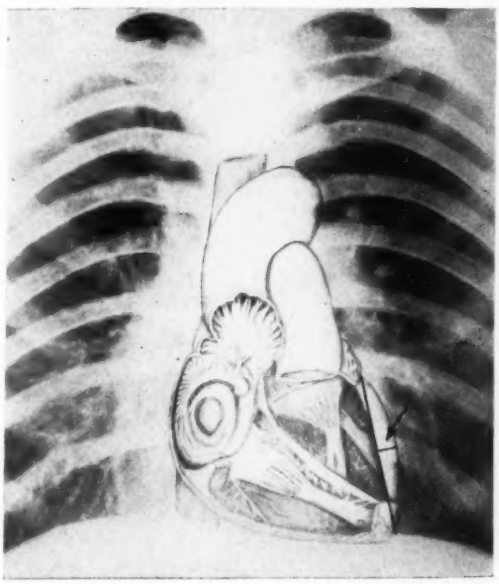

Fig. 1.—A perpendicular (arrow) erected on a line joining the auriculoventricular sulcus and the apex, from the point of greatest salience of the left ventricle, measures the thickness of the left ventricular myocardium.

Although slight difficulty may be experienced in locating these points on the film, they are readily defined on roentgenoscopic examination. The auriculoventricular sulcus is a groove containing a variable amount of fatty tissue, and, roentgenographically, fat is less dense than muscle. The silhouette will, therefore, show a zone of diminished opacity in the region of the sulcus. The landmark for measurement is located in this zone, at the point of the first break in the contour of the left ventricle.

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In locating the apex, confusion may be avoided by recalling that the heart is more or less pyramidal in shape, and that the apex of a pyramid is the thinnest point opposite the base. The landmark for measurement, therefore, is the most pointed part of the heart shadow.

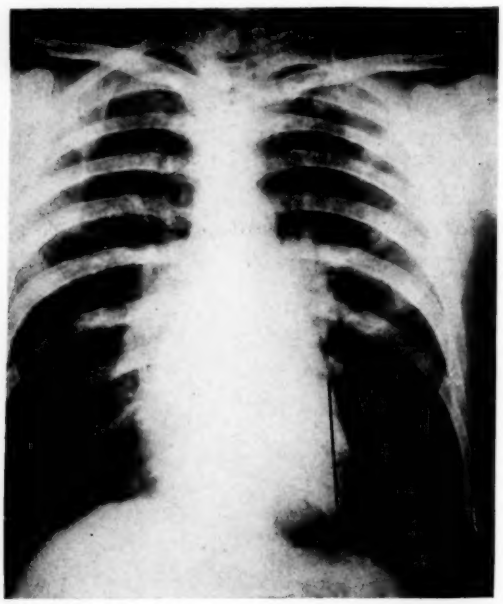

Fig. 2.—Comparatively thin-walled left ventricle in a case of mitral stenosis.

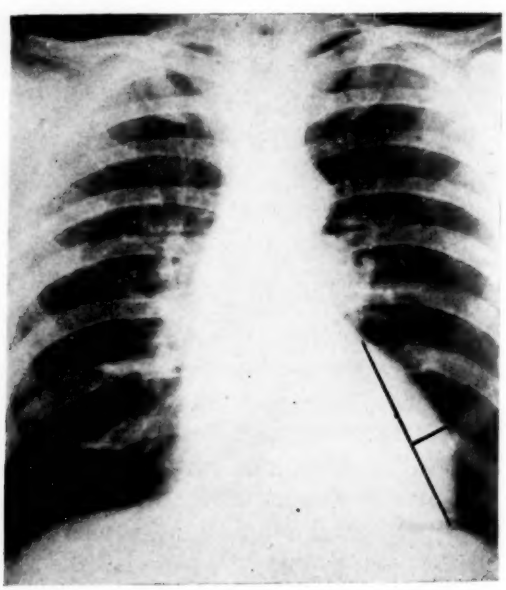

Fig. 3.—Hypertrophy of the left ventricle in a case of hypertensive heart disease.

In a series of 100 unselected cases in which roentgenologic measurements were compared with those reported by the pathologist at necropsy, there was an *average* discrepancy of one millimeter. For practical purposes, this is not significant. Individual variations occurred mostly in hypertrophied hearts, but left ventricular hypertrophy was clearly demonstrated by roentgenologic measurement. When variations were found, the post-mortem measurement was always greater than the one obtained during life, probably because of a difference in the state of tone of the heart muscle.

Figs. 2 and 3 are typical of the series and serve to illustrate the roentgenologic demonstration of left ventricular hypertrophy.

Knowledge of the thickness of the wall of the left ventricle is of assistance in the differential roentgenologic diagnosis of cardiac enlargement.[2] The electrocardiograms of the patients in this series were reviewed with the thought that a correlation might possibly be shown between left ventricular hypertrophy and left axis deviation. No such relationship could be demonstrated. Roentgenologic measurement, however, was sufficiently close to that obtained at necropsy to establish this procedure as a reliable index of left ventricular hypertrophy.

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EXPERIMENTAL METHODS FOR PRODUCING CHRONIC, PROGRESSIVE, CORONARY ARTERIAL OCCLUSION

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STUDY of the coronary circulation in coronary arterial disease has been limited because of inability to produce experimental obstruction of coronary arteries simulating that which occurs clinically in coronary sclerosis and syphilitic aortitis. This report concerns experimental methods that have been devised and used to produce chronic, progressive, coronary arterial obstruction in dogs. The details of the studies on the coronary circulation have been reported elsewhere.[1, 2, 3]

Halsted[4] devised a method of progressively occluding arteries as large as the abdominal aorta, but this method was never applied to small arteries, such as the coronary arteries. Goldblatt and his associates[5] designed and successfully used a small silver clamp for gradually occluding the renal arteries to produce hypertensive cardiovascular disease in dogs and monkeys. Because of the anatomic differences between the renal and coronary arteries, the Goldblatt clamp could not readily be used on the latter.

Beck, Tichy, and Moritz[6] experimented with a number of methods of occluding the main coronary arteries in multiple stages. Attempts to obtain progressive occlusion of main branches by encircling the arteries with fascial and periosteal bands, by using sclerosing substances, and by using wires for electrocoagulation were unsuccessful. Small bands made from sheet silver were successfully used to occlude main arteries in two or three stages. However, this method was not ideal because of the difficulty in locating the bands at the time of reoperation and in judging the degree of occlusion when the bands were compressed. In an attempt to simplify the procedure, two modifications of a screw clamp are described for progressively occluding coronary arteries.

Fig. 1*A* shows the first type of clamp used. The screw mechanism and general construction are similar to those of the Goldblatt clamp. The parts are machined from pure silver. The U-shaped part of the clamp is placed around the vessel to be constricted, and the screw mechanism with the compressing plate fits into the grooves as shown. Drill holes are placed so that these two parts can be tied together to prevent their becoming disengaged. The screw mechanism can be locked each time it is tightened, preventing spontaneous loosening of the screw.

The operations for applying and using the clamps are as follows: Moderately large dogs are selected, weighing from 12 to 15 kg. Under

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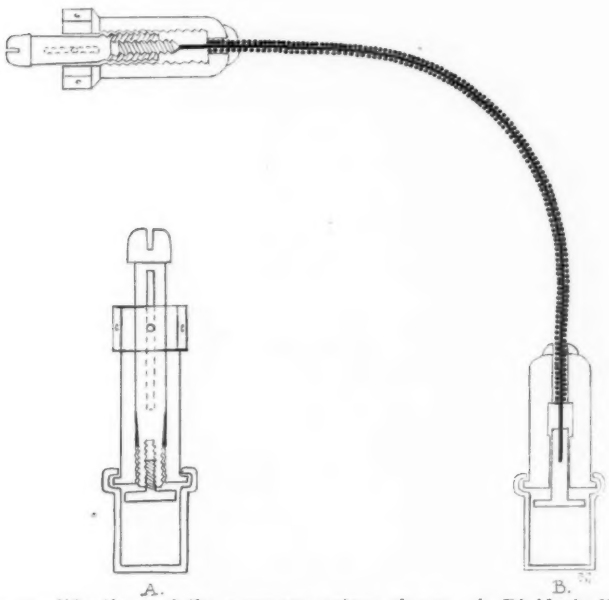

Fig. 1.—Two modifications of the coronary artery clamp. *A*, Rigid shaft; *B*, flexible shaft. (Reproduction is twice actual size.)

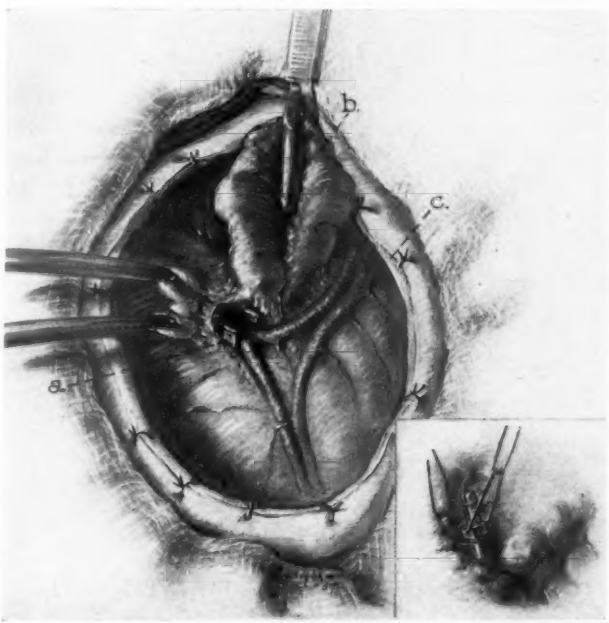

Fig. 2.—Exposure for the application of clamp to the common left coronary artery. *a*, Common left coronary artery with the lower part of the clamp in place; *b*, left auricular appendage; *c*, pericardium sutured to intercostal bundles. The inset shows compressing mechanism of clamp in place and anchored to the pulmonary artery.

intratracheal ether anesthesia, the anterior two-thirds of the left fifth rib and costal cartilage are removed, and the pleura is opened. The phrenic nerve is dissected free from the pericardium, and the latter is opened by a transverse incision near the base of the heart. The cut edges of the pericardium are carefully sutured to the periosteal edge of the chest wall wound (Fig. 2), in order to seal off the pleural space and permit opening the pericardium subsequently without opening the pleural cavity. By gentle traction on the left auricular appendage and the adipose tissue in the groove between the pulmonary artery and aorta,

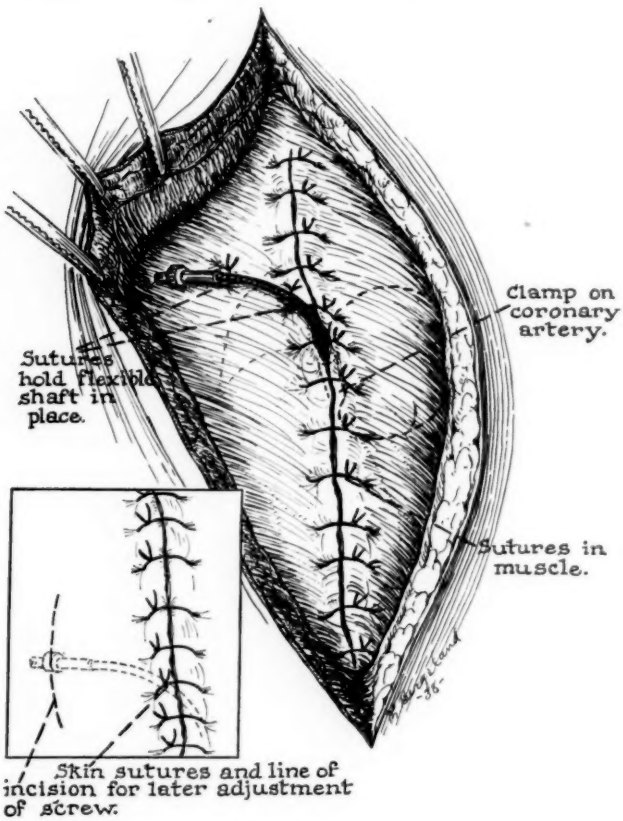

Fig. 3.—Clamp with flexible shaft in place, with the flexible end brought out under the platysma muscle.

the origin of the left coronary artery can be exposed and isolated by careful dissection. In about 30 per cent of dogs, the common left coronary artery is of sufficient length that a portion long enough to permit application of the U-shaped part of the clamp above the origin of the septal artery can be isolated. The two parts of the clamp are engaged and tied together. If dogs are used that have previously had the right coronary artery occluded, all of the remaining, normal, arterial blood supply can be controlled by one clamp. The screw sheath is

anchored in such a position that there is no torsion on the artery. The auricular appendage is sutured to the pericardium in order to prevent the tip from becoming adherent to the clamp. The purpose of the long screw sheath is to make it possible to tighten the clamp without again exposing the artery. The wound is closed in layers, approximating only the latissimus dorsi, platysma, and skin. The same exposure is used in applying the clamp to either the circumflex or descending branch of the left coronary artery. A similar approach from the right side is used in applying the clamp to the right coronary artery.

Reoperations for tightening the clamp can frequently be done under local anesthesia through a small incision.

Certain difficulties which were encountered with this clamp led to a further modification (Fig. 1*B*). In this modification of the clamp, a flexible cable of stainless steel is interposed between the screw mechanism and the clamp. A somewhat similar clamp was simultaneously developed by Blum, Schauer, and Calef.[7]

The second type of clamp is applied much as the first. The flexible outer shaft and plunger may be constructed in various lengths, and the control may be placed at any reasonable distance from the point of compression without any loss of mechanical efficiency. Reoperations are simple and are carried out under local anesthesia. We have found it convenient to bury the screw sheath beneath the skin and the platysma by tunneling a few centimeters from the operative site at the time of the original operation (Fig. 3). To avoid infection, we prefer not to bring the shaft out through the skin. Some animals in our laboratory have had clamps on their coronary arteries for over two years.

SUMMARY

An experimental method for producing slow, progressive occlusion of coronary arteries is described. Studies on such preparations are presented in other papers.

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THE SIGNIFICANCE OF VASCULAR HYPERREACTION AS MEASURED BY THE COLD-PRESSOR TEST*

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THE majority of individuals with essential hypertension and some with usually normal blood pressure manifest unusual lability and marked reactions of blood pressure to various internal and external stimuli. This suggests that the mechanism for regulating blood pressure which is possessed by these individuals is hyperreactive. The cold-pressor test is a satisfactory method of determining the reactivity of the blood pressure. The test consists in measuring the reaction of the blood pressure to a standard cold stimulus.[1]

In this paper the expression, "person with usually normal blood pressure," will appear frequently. It means a person who does not have persistent hypertension, one whose blood pressure remains within normal limits unless caused to rise by a stimulus. Later in this paper such persons will be divided into the classes called "normal hyporeactors" and "normal hyperreactors."

THE TEST

Precautions.—At the Mayo Clinic we perform the test with the subject supine. If other positions are used, the effect of posture must be taken into account in evaluating the results. Sitting or standing will cause elevation of the basal blood pressure, especially of the diastolic pressure, and the hydrostatic effects of sitting or standing usually will decrease the reaction to the cold water, particularly if the subjects have hypertension.

It is well to describe to the patient the nature of the test at the beginning of the period of rest, so that he may not be apprehensive. The temperature of the water should not be more than one degree above or below 4° C., and its temperature should be measured just before the hand is plunged into it.

Inasmuch as drugs which cause vasodilation and sedation may reduce the response to the standard stimulus, the subject should not have taken any of these drugs within twenty-four hours before the test is performed. Such slowly eliminated sedative drugs as the bromides may affect the response longer than twenty-four hours after their use has been discontinued.

Technique, interpretation, and uniformity.—The subject is allowed to rest supine, as has been said. The room is quiet and the period of rest

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*The term "vascular" refers to that part of the vascular system concerned with the regulation of blood pressure.

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lasts for twenty to sixty minutes. Twenty minutes is a satisfactory period of rest for persons whose blood pressure is normal. Several measurements of the blood pressure are made until an approximately basal level has been reached. If hypertension is present, a longer period of rest may be necessary to establish a basal level. The blood pressure of a few patients who have severe, essential hypertension will remain fixed at high levels, and a basal level cannot be secured even after several hours of rest.

With the subject still supine, and with the cuff of the sphygmomanometer on one arm, the hand on the opposite side is immersed in ice water (4° C.) to a line just above the wrist. With the hand still in the water, readings of blood pressure are taken at the end of thirty and of sixty seconds. The highest of the two readings obtained while the hand is in the ice water is taken as an index of the response. The hand is removed from the ice water as soon as the measurement at sixty seconds has been made, and measurements are made every two minutes thereafter until the blood pressure has returned to its previous basal level.

The maximal response frequently occurs within thirty seconds. The blood pressure of subjects whose pressure is usually normal returns to the basal level within two minutes after the hand has been removed from the water. In the presence of established hypertension, the return of the blood pressure to the basal level may be delayed.

The diastolic response to the stimulus is a more reliable index of vasoconstriction than the systolic response, but the amount of error will be reduced if both the systolic and diastolic responses are considered in evaluating the result of an individual test. Inasmuch as the test is a measure of vasoconstrictor response, the systolic measurement alone is of questionable value in determining whether the subject has a hyperreactive vasoconstrictor mechanism. As to what constitutes a significant response, analysis of the results of a large number of tests has shown that an elevation, above the basal level, of more than 20 mm. of mercury in systolic pressure *and* of more than 15 mm. in diastolic pressure indicates a hyperreactive type of response to the stimulus. If the maximal reading obtained in a case in which the blood pressure usually is normal is 140 mm. of mercury, systolic, and 90 mm., diastolic, the subject can be considered, even more certainly, to have a hyperreactive vasoconstrictor mechanism.

It is now generally conceded that quick rises in blood pressure, unassociated with cardiac acceleration or increased cardiac output, are brought about by vasoconstriction, which produces an increase in peripheral resistance. It can be assumed, therefore, that such a rise in blood pressure, resulting from a given stimulus, is an index of vascular reactivity. For this reason, it is believed that the response of the blood pressure to the cold-pressor test is an index of vascular reactivity.

The cold-pressor test should be considered a clinical test. There may be some variation of the range of response on repeated tests, but, if care is taken to reproduce the same basal conditions and to carry out the test in exactly the same manner on each occasion, the variation will be minimal. After repeating the test many times on the same individuals, I found that the results were remarkably constant, and the test has proved suitable for practical use. Ayman and Goldshine,[2] using the same technique which I have described, found that the type of response, in general, was fairly constant on repeated tests, although there was considerable variation in the response of some of their patients. Some of the variation observed by Ayman and Goldshine might have been caused by the effects of posture on the blood pressure, for they carried out the test with the subjects sitting, rather than supine. Pickering and Kissin[3] also found that the reaction of the blood pressure to a standard cold stimulus was fairly constant in their small group of subjects.

EXPERIENCE WITH THE TEST AND INFERENCES DERIVED THEREFROM

I have made three previous reports on the results obtained with the cold-pressor test.[4, 5, 6] Up to the present, this test has been applied by me, or under my direction, approximately 5,000 times, to 1856 persons, of whom 1015 usually had normal blood pressure and 841 had essential hypertension. The data are summarized in Table I. In the entire group with usually normal blood pressure the mean increase was 16.2 mm. for the systolic pressure, and 13.2 mm. for the diastolic. The group with usually normal blood pressure is divided into hyporeactors and hyperreactors on the basis of, respectively, a rise less than, or more than, 20 mm. in systolic *and* 15 mm. in diastolic blood pressure. Approximately 85 per cent of subjects with usually normal blood pressure fell in the group of hyporeactors.

TABLE I

SUMMARY OF DATA ON COLD-PRESSOR TEST

SUBJECTS		MEAN RISE IN BLOOD PRESSURE MM. OF MERCURY	
TYPE	NUMBER	SYSTOLIC	DIASTOLIC
Blood pressure normal			
Hyporeactors	859	12.4	10.1
Hyperreactors	156	31.2	27.5
Patients with essential hypertension	841	46.6	30.9

The effect of age on response.—Pickering and Kissin stated that, among patients with usually normal blood pressure, the response of the pressure to stimulation by cold increases with age, and that, among elderly persons, the response of those who have essential hypertension is not greater than is that of patients who usually have normal blood pressure. However, these investigators studied only nine elderly subjects with usu-

ally normal blood pressure, and only twelve patients with essential hypertension. In a communication to Ayman and Goldshine, Pickering stated that, generally, the blood pressure was measured for only ten minutes before the test was performed, and that many of his patients had been in bed for days or weeks before the test was done. It is probable that in the investigations of Pickering and Kissin the blood pressure of some of their patients with hypertension failed to reach a basal level. Also, it is possible that some of the subjects whom Pickering and Kissin regarded as having a usually normal blood pressure actually had essential hypertension, but prolonged rest in bed had brought about a lowering of their blood pressure to normal. Furthermore, these investigators did not carry out the test in exactly the same manner as that employed by me. As far as I know, whenever the test has been carried out exactly according to the technique I have described, the results have agreed with mine. The response of the blood pressure to the cold-pressor test, according to decades of life, is shown in Table II and Fig. 1. Among persons with usually normal blood pressure, there is an increase in the mean systolic response with increasing age, but this also occurs among patients with essential hypertension. The mean diastolic response of young children with usually normal blood pressure is increased, but that of patients with usually normal blood pressure who are more than fifty years of age is decreased. The mean diastolic response of patients with essential hypertension remains about the same at all ages.

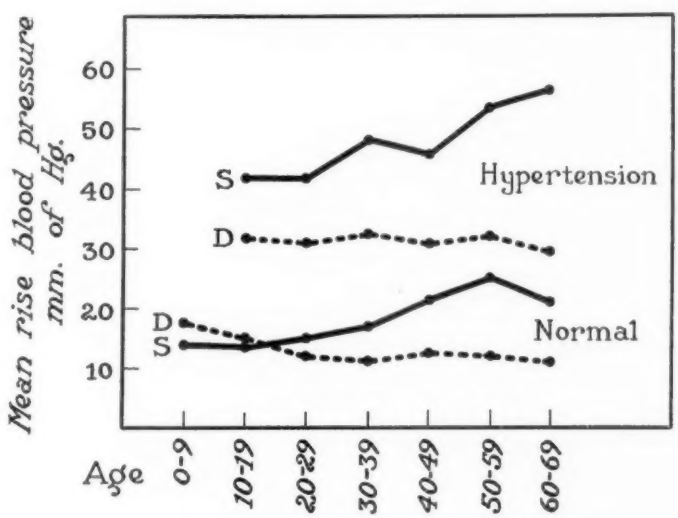

Fig. 1.—Effect of age on response to cold-pressor test.

Vascular hyperreactivity and essential hypertension.—According to data which I have been able to obtain from the literature,[7, 8, 9, 10, 11] other workers have performed the cold-pressor test, or a modification of it, on 827 subjects with usually normal blood pressure and on 276

patients with essential hypertension. Combined with my group, this makes a total of 1842 subjects with usually normal blood pressure and 1,117 patients with essential hypertension on whom the cold-pressor test, or a modification of it, has been performed. The results show that the mean response of the blood pressure of patients with essential hypertension to a standard stimulus is from two to six times greater than that of subjects with usually normal blood pressure. These data indicate that vascular hyperreactivity, as measured by the cold-pressor test, probably plays an important role in the majority of cases of essential hypertension. The vascular hyperreactivity of some patients with essential hypertension is extreme (Fig. 2). Of those subjects who at one time were normal hyperreactors but later developed essential hypertension, the range of response to the cold-pressor test was increased as the hypertension developed.

TABLE II

EFFECT OF AGE ON THE RESPONSE TO COLD-PRESSOR TEST

AGE, YEARS	TOTAL SUBJECTS		SYSTOLIC RESPONSE		DIASTOLIC RESPONSE	
	BLOOD PRESSURE NORMAL	PATIENTS WITH HYPERTENSION	BLOOD PRESSURE NORMAL	PATIENTS WITH HYPERTENSION	BLOOD PRESSURE NORMAL	PATIENTS WITH HYPERTENSION
0- 9	128	0	14.8		16.4	
10-19	325	26	13.8	43.0	14.2	33.1
20-29	149	87	15.3	42.9	13.1	31.1
30-39	163	290	15.5	46.9	13.8	30.7
40-49	124	191	18.1	42.4	14.1	29.6
50-59	78	195	19.7	49.2	12.5	32.6
60-69	48	52	16.8	56.5	8.6	28.6

Vascular hyperreactivity and latent hypertension.—I have observed more than 100 individuals in the later decades of life who had hypertensive changes in the retinal arterioles but whose blood pressure was usually normal and who gave no history of hypertension. The blood pressure of many of these patients was taken over a number of years, and they are known not to have had hypertension. All gave evidence of having a hyperreactive vascular system, as measured by the cold-pressor test. I have designated these subjects as having "latent hypertension," and have attributed the vascular changes to the vascular hyperreactivity and not to hypertension earlier in life.[12]

There is a significant group of persons who are known to have had hypertension but whose blood pressures no longer are elevated, usually because of cardiac failure. Schwab and Curb[13] and Briggs and Oerting[14] have studied the reactions of such patients to the cold-pressor test and have found that the majority give a hypertensive type of reaction during the period when the blood pressure usually is normal. Consequently, it may be said of these patients that the hyperreaction to the cold-pressor test is evidence of previous hypertension which is temporarily latent.

Vascular hyperreactivity and the prehypertensive state.—Some of a large number of healthy individuals with usually normal blood pressure have given evidence of vascular hyperreactivity, as measured by the cold-pressor test. I believe that this type of vascular hyperreactivity represents a "prehypertensive" phase of the syndrome which is designated as essential hypertension. The evidence on which this contention is based is as follows: 1. The hyperreactivity of the blood pressure of the normal hyperreactor is of the same type, and frequently of the same degree, as that which is characteristic of 95 per cent of individuals with essential hypertension. 2. Individuals who are known to have had hypertension, but whose blood pressure has been reduced to normal by cardiac failure, or some other factor, give a hyperreactive response to the cold-pressor test similar to that of the normal hyperreactor or the person with hypertension. 3. The incidence of hyperreactors among children approximates the combined incidence of hypertension and hyperreactors among adults.[15] 4. Subjects with usually normal blood pressure who are hyperreactors generally come from families in which there is a high incidence of hypertensive cardiovascular disease, whereas subjects with normal blood pressure who are

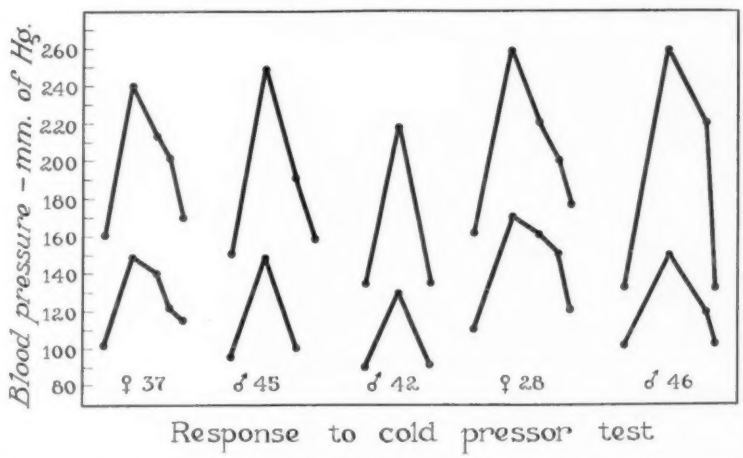

Fig. 2.—Extreme hyperreactivity of blood pressure in cases of essential hypertension.

hyporeactors generally do not.[16] Furthermore, investigation of the response to the cold-pressor test of 256 members of thirty families revealed that when both parents gave normal responses to the test none of the children were hyperreactors or had hypertension. When one parent had hypertension, or was a hyperreactor, and the other gave a normal response, 43 per cent of the children were hyperreactors. When both parents were hyperreactors, 95 per cent of the children were hyperreactors. Briggs and Oerting,[17] in their application of the cold-pressor test to a group of 233 patients receiving prenatal care, found that the offspring of parents, both of whom had hypertension, always

gave hyperreactions, but that only two hyperreactors were found among subjects with no family history of hypertension. 5. Six years have elapsed since the original sixty-six subjects with normal blood pressure were first subjected to the cold-pressor test. Recently, I have obtained satisfactory information regarding the present status of the blood pressure of all but three of the twenty-four originally normal hyperreactors and of twenty-eight of the forty-two originally normal hyporeactors. So far, I have not learned of a normal hyporeactor who has developed essential hypertension, whereas 38 per cent of the originally normal hyperreactors are known to have developed essential hypertension.

The group dealt with under "5" in the foregoing paragraph is admittedly too small, and the time since the original tests were made is too short to justify the declaration that a great many hyperreactors to the cold-pressor test will eventually have essential hypertension, and that the hyporeactors generally will not. Another ten years must pass before data can be obtained which will prove or disprove this contention. Consequently, the general use of the cold-pressor test to predict the future development of hypertension is not advocated at present. My primary purpose in this work was not to develop a method for predicting that hypertension would appear in the future in a given case, but to show that there is an antecedent, or prehypertensive, phase of essential hypertension which has as its characteristic the same type of vascular hyperreactivity that is present in essential hypertension. This should be considered in attempting an explanation of the etiology of essential hypertension.

Vascular hyperreactivity to cold test correlated with that to first measurement of blood pressure.—In another study I obtained significant collateral evidence that there is an antecedent phase of essential hypertension which is manifested by hyperreaction of the blood pressure to stimulation. A more detailed report of this study is being presented elsewhere. I noted in many instances a correlation between the "ceiling," or maximal elevation, of the blood pressure of a patient to the cold-pressor test and the first measurement of blood pressure made on the same patient in the clinic office. This correlation was noted also by Ayman and Goldshine in their work with the cold-pressor test. The first measurement of blood pressure in the clinic is generally made by a physician with whom the patient is unacquainted, and the surroundings are strange. Consequently, the patient's blood pressure represents a reaction to nervous stress, which is, in effect, a psychic pressor test. Data have been obtained on approximately 1500 patients (some of whom are included in Table III) with originally normal blood pressure who returned to the clinic ten and twenty years after their first visits. It was found that the majority of patients whose blood pressure, under nervous stress, was in the upper range of normal (140

to 150, systolic, and 85 to 100, diastolic) subsequently had hypertension, whereas only a small number (3.6 per cent) whose blood pressure was hyporeactive subsequently had hypertension (Table III). To state this in a different way, of 206 patients who recently had hypertension, 86 per cent gave evidence of hyperreactivity of the mechanism for regulating blood pressure ten to twenty years previously, although they did not have hypertension at that time, and the majority did not have it until a number of years had elapsed. These data probably show that, among subjects with normal blood pressure, excessive response of the systolic and diastolic blood pressure to nervous stress is usually indicative of a prehypertensive stage of essential hypertension. The correlation between this type of reaction and the reaction to the cold-pressor test indicates that the significance of both is the same.

TABLE III

REACTION OF BLOOD PRESSURE TO NERVOUS STRESS* CORRELATED WITH THE SUBSEQUENT DEVELOPMENT OF HYPERTENSION

SUBJECTS		HYPERTENSION 10 TO 20 YEARS LATER	
CLASSIFICATION	NUMBER	NUMBER	PER CENT
Blood pressure normal			
Hyporeactors	1018	37	3.6
Hyperreactors	239	169	70.7

*First measurement of blood pressure made in clinic.

CONCLUSIONS

1. The cold-pressor test is an index of vascular reactivity.

2. Vascular hyperreactivity, as measured by the cold-pressor test, is an important etiologic factor in essential hypertension.

3. Vascular hyperreactivity may occur, however, as an inherited characteristic of persons who do not have hypertension. The vascular hyperreactivity of many of these persons represents an antecedent or a latent phase of essential hypertension.

4. As yet, the percentage of originally normal hyperreactors who will have hypertension is unknown. Thirty-eight per cent of twenty-one originally normal hyperreactors have developed hypertension within six years, whereas none of the normal hyporeactors have developed hypertension in this period.

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THE CARDIOMENSURATOR, AN INSTRUMENT FOR THE DETECTION OF CARDIAC ENLARGEMENT BY DIRECT CORRELATION OF THE TRANSVERSE DIAMETER OF THE HEART WITH BODY WEIGHT AND HEIGHT

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ROENTGENOLOGICALLY, cardiac mensuration remains unstandardized. Undoubtedly, the difficulty lies in part in the fact that one is attempting to measure a three-dimensional object by means of a single roentgenogram, from which, under ideal conditions, only two dimensions can be obtained. Furthermore, certain methods have been commonly used because of their simplicity, rather than because they have been shown to employ criteria which ensure a high degree of correlation. This is true of the cardiothoracic ratio, for which only the transverse diameter of the heart and the internal diameter of the chest are required. It is also likely that many cardiac measurements are now being made from routine chest roentgenograms which are obtained in very short periods of time (less than one-tenth of a second) at the end of a maximum inspiration. Cardiac shadows in such roentgenograms will vary in size depending upon the phase of cardiac contraction, as well as upon the position of the diaphragm.

It would appear desirable to take routine roentgenograms of the heart with a technique which differs considerably from that employed in making the usual chest radiograph. Improvements in roentgenographic equipment during recent years have resulted in a highly developed technique for pulmonary detail. This has militated against a standardized technique for cardiac measurements. For a satisfactory roentgenogram of the heart, the exposure should not be made at the end of a full inspiration, for this places the diaphragm in a low position if the person is a vigorous adult, and the patient will be unable to duplicate this when cardiac failure, with a decrease in vital capacity, has supervened. To obtain a suitable radiograph, the patient should simply be instructed to stop breathing when requested; the signal is given during quiet tidal breathing at the end of a normal inspiration. Less cooperation is required in cases of aged or very youthful subjects with a routine method of this type.

Ideally, the exposure of the film should be timed to secure maximum size of the heart (end of diastole), but in practice this is a difficult, complex procedure. The simple expedient of a prolonged exposure time (to

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include an entire cardiac cycle) does not fulfill the requirements for ensuring that diastolic size will be recorded. Actual timing in relation to the cardiac cycle is necessary if diastolic size is to be obtained. Simple tests show that exposure of a mobile object, such as the heart, beginning during a period of rest and continuing during a phase of movement, casts a relatively sharp shadow of the outline, whereas one beginning during a phase of movement is commonly blurred. To illustrate, a pendulum of lead may be radiographed with an exposure comparable to that used for the chest, and if the exposure begins at the end of its swing (during a quiet period) a sharp margin, corresponding with the end of the swing, is noted. If the exposure is as short as that used for the chest today, the outline is indistinct whenever the exposure is started while the pendulum is swinging (Fig. 1). There is an additional blurring effect in some of the exposures of the heart which are made during routine chest roentgenography. An exposure beginning when the heart is at or near its maximum size will have sharper contours than a similar exposure made when it is smallest. This is because of the fact that, when the greater part of the exposure occurs at a time when the heart is small, the silver emulsion adjacent to the borders of the heart has been considerably affected by the radiation, leaving a comparatively small number of silver grains to be affected by the remainder of the exposure, while the heart is increasing in size.

The remaining requirements for radiography of the heart are better understood. To prevent undesirable distortion, teleoradiography is employed, using target-film distances of six feet, or more, with the patient in the erect position and the anterior aspect of the chest applied to the cassette. Roentgenograms made with the patient recumbent and with his back applied to the cassette are undesirable both because of the distortion produced and because of the effect of the altered position of the diaphragm upon cardiac shape and size. Care also should be exercised to prevent the occurrence of changes in cardiac size resulting from Valsalva effects (attempting to expire against a closed glottis). These effects, fortunately, are not likely to occur if the exposure is made during tidal breathing, but often are observed when the exposure is made at the height of inspiration. The patient, in his desire to cooperate, may inspire maximally and, to prevent egress of air, may close the glottis, subsequently relaxing the inspiratory set of the thorax. A marked decrease in both the measurements of length and area will result in such cases, rendering the detection of early enlargement of the heart very difficult.

A roentgenogram suitable for cardiac measurements, fulfilling all of the necessary conditions, may be obtained by two radically different methods. A radiograph may be made while the heart is in diastole by timing the exposure by means of an electrical circuit energized by amplified heart sounds or the amplified R wave of the electrocardio-

gram. This is a complicated method which cannot be adapted to routine use at the present time. The second method employs the kymograph. This method is simple, requires no special amplifying circuit, and is now purchasable as a commercial product. No special skill is required for its operation, and it requires no more time to secure a radiograph by this method than by the Bucky technique. Fast screens are necessary in order to obtain the required speed for teleoradiographs. The method has the advantage of recording both systolic and diastolic size, and, in addition, gives useful information concerning the strength and quality of the pulsations.

Granting that roentgenograms have been obtained with proper technique, how may one separate the abnormal and questionably abnormal hearts, which require further study, from those obviously normal? An instrument* has been devised which enables one to make

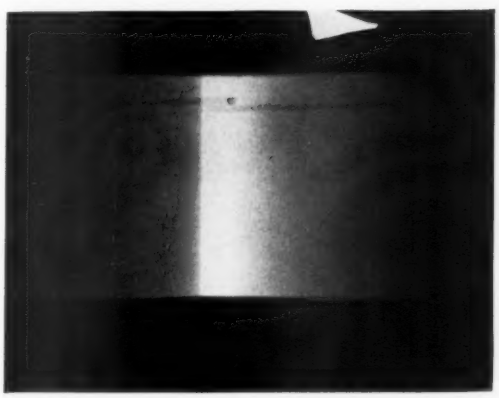

Fig. 1.—Radiograph of a square pendulum (period slightly less than 1 sec.). The exposure began while the pendulum was at the right end of its swing (during a period of relatively no movement), and continued during its swing toward the observer's left. Note the sharp margin of the square on the right and the indistinct margins on the left. In this latter region the silver emulsion had been affected by direct exposure prior to the swing of the pendulum to this position, leaving a much decreased amount to cast the shadow of the pendulum during this portion of its swing.

a direct estimate of the degree of cardiac enlargement. The mechanics of the instrument are based upon the relatively high correlation between cardiac size and size of the body. A number of investigators (Hodges and Eyster,[2] Bainton,[1] Ungerleider and Clark,[3] and others) have shown that the transverse diameter can be correlated with weight (directly) and height (inversely). The principle of the present instrument is based upon this correlation, and the estimate may be made directly from the roentgenogram by stretching an elastic cord across the maximum transverse diameter of the heart. No computations regarding heart size are required, but the weight of the person is

*To the United States Rubber Products, Inc., the writer is indebted for the opportunity to test several of their elastic cords, one of which proved to be ideal for use in preparing the instrument. A kymographic grid was loaned by the Liebel-Flarsheim Co., whose close cooperation has been most helpful.

divided by his height (since the latter is inversely related to cardiac size) to obtain an index of the same kind as that of Ungerleider and Clark. The mathematical principle upon which the present instrument depends was taken from their work. Their mathematical data are considered as reliable as any available at this time, because the roentgenograms were obtained at the midrespiratory level with the patient erect, and observations were made on nearly 1,500 subjects.

The instrument consists of a transparent rule, through which the cardiac shadow may be visualized, with a rubber cord along its upper margin. The left end of the cord is fixed to the transparent rule, and its right end is fastened to a collar which slides along the length of the rule. The rule has three scales upon it: (a) a true centimeter scale (uppermost); (b) a scale of heart indices, i.e., the weight in pounds divided by the height in inches (middle scale); and (c) a scale of percentages, indicating the degree of enlargement.

It is essential that the elastic cord stretch uniformly throughout its length. It requires no scale, but there is a small metallic rider, with a central hole, which slips freely along the length of the cord. The free mobility of the rider permits placing it at any point along the elastic cord, and, when once placed, it retains its relative position regardless of the degree of stretching, i.e., if placed at the center of the elastic cord under low elastic tension, it will be at the center of the elastic under all higher tensions.

Its use is demonstrated by the following illustrative case. A young woman who was examined because of long-standing hypertension weighed 125 pounds and was 5 feet, 3 inches in height. When her weight of 125 pounds was divided by 63 inches, an index of 19.9 was obtained. The collar of the instrument was moved along the transparent rule so that the right end of the elastic cord corresponded with this index on the rule. The rider of the elastic cord was then moved along the cord until it corresponded with 0 on the percentage scale. The elastic cord was next stretched, holding the instrument in front of the roentgenogram so that the ends of the cord corresponded with the right and left borders of the heart (Fig. 2). A direct reading of the position of the rider with respect to the percentage scale was then made (in this case, 12.0 per cent). This reading of 12 per cent represents an increase in the length of the transverse diameter over that of a normal person of the same size.* Since the instrument is provided with a true centimeter scale, one may record the transverse diameter of the heart at the same time that the percentage increase is obtained; these data may be included in the report, permitting comparison with clinical measurements. Without resorting to computations, one may

*The normal transverse diameter of the heart for an individual of this size may be found quickly by locating the point along the true centimeter scale which corresponds with the index 19.9 (11.9 cm. in the present case).

measure (a) the transverse diameter of the heart in centimeters, (b) read off any increase in the length of this diameter in per cent, and (c) find out what the transverse diameter of the heart of a normal person of corresponding size should be.

The normal is illustrated in Fig. 3. The subject was a healthy young man whose radiograph was made solely because he had been accepted for employment at a type of work which involved industrial hazard. His weight (185 pounds) divided by his height (70 inches) yielded an index of 26.4. The elastic cord was stretched so that the maker at the right end was opposite this index, and, while in this position, the small rider on the cord was slipped opposite the 0 on the percentage scale. The cord was then stretched across the roentgenogram so that the beginning marker of the cord was at the right border of the heart and its other end at the left border. The rider on the cord now fell

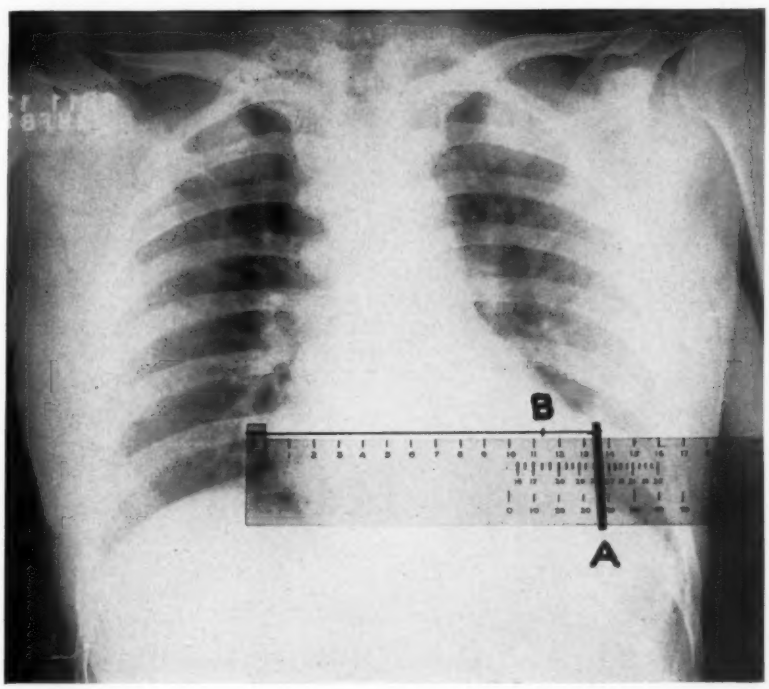

Fig. 2.—Demonstrating the use of the instrument in a case of persisting hypertension in a youthful person. The index of 19.9 in this case was obtained by dividing the weight (125 pounds) by the height (63 inches). The steps in making the determination are as follows: 1. Place the sliding collar (*A*) so that its inner margin is opposite the index 19.9. Opposite 19.9 on the index scale is 11.9 cm. (predicted normal for a person of this weight and height).

2. Place the small rider (*B*) over zero on the percentage scale.

3. Extend the elastic cord so that the right border of the heart is at one end of the elastic band and the left at the other.

4. Read on the percentage scale (lowermost) 13.3 per cent.

5. Measure the transverse diameter of the heart from the centimeter scale (uppermost), keeping the instrument in the same position.

Results show the transverse diameter of the heart to be 13.3 cm.; the predicted normal for a person of this height and weight, 11.9; and the percentage of increase, 12.0.

opposite 1 (one) on the percentage scale, indicating a size only 1 per cent above the predicted normal, which is within the limits of normal variation.

It is hoped that the ease with which the instrument may be employed will result in its daily use for measuring hearts in all posteroanterior teleoroentgenograms, and that it will replace the cardiothoracic ratio. It should serve as a quick means of selecting patients who need more detailed study. When the value obtained exceeds 5 per cent of the estimated normal, or when the heart appears to be of normal size, but the patient gives a history suggesting the possibility of heart disease, further investigation should be made. In such cases one should obtain (a) left or right oblique teleoroentgenograms, (b) esophagrams, and (c) heavy-exposure roentgenograms at a short tube-object distance (30 inches) during tidal breathing, with a short exposure, for the de-

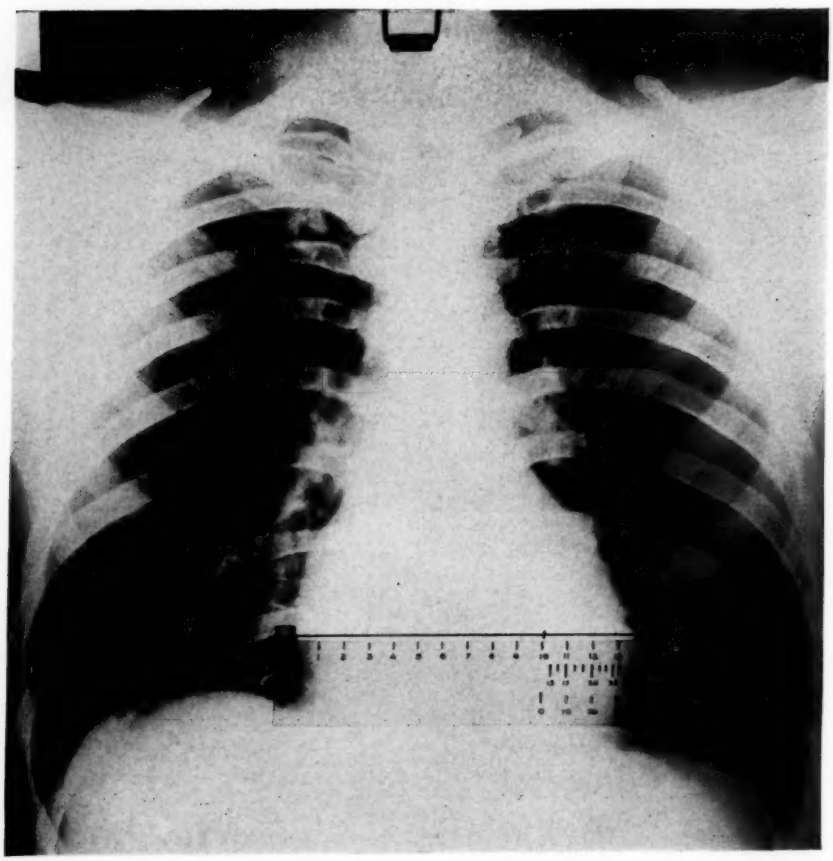

Fig. 3.—Showing use of the instrument in measuring a normal heart. The person's weight is 185 pounds; height, 70 inches; and heart index, 26.4. With the sliding collar placed opposite 26.4, the predicted normal transverse diameter is 13.8 cm. By stretching the cord across this diameter of the heart after placing the rider opposite zero on the percentage scale (lowermost), it is found that the transverse diameter is 13.9 cm., and the percentage increase, 1.

tection of calcification. Careful fluoroscopic examination for evidence of calcification is essential in all cases.

CONCLUSIONS

1. The cardiomensurator was devised to facilitate detection of enlargement of the transverse diameter of the heart. Its principle is based upon a correlation with body weight and height.

2. This instrument gives the following information: (a) the percentile increase in the length of the transverse diameter; (b) the average length of the transverse diameter of normal individuals of the same weight and height, for comparison, and (c) the transverse diameter of the heart in centimeters.

3. This is accomplished without resorting to computations or consulting graphs.

4. The length of time required for the use of the instrument after the weight and height of the patient are known and the index obtained is a matter of a few seconds; in fact, it can be accomplished as quickly as the elastic cord can be stretched across the cardiac shadow after setting the rider.

5. It is hoped that this simple method will supplant the cardiothoracic ratio, which is known to be inaccurate because of the lack of linear correlation between the transverse diameter of the heart and the internal diameter of the chest.

6. The instrument does not pretend to afford a means for complete mensuration of the heart, but it should prove valuable in cases in which detailed study is not required.

7. It is suggested that teleokymography provides an easy method of obtaining the transverse diameter of the heart in diastole, and it eliminates errors resulting from cardiac contraction.

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A STUDY OF CARDIOVASCULAR DISEASE IN CHARLESTON, S. C., BASED UPON NECROPSY STATISTICS*

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A CLINICAL and necropsy study of fatal cardiovascular disease in Charleston, S. C., covering the period from 1928 to 1938, has been completed by the authors.[1] This paper presents a parallel study covering a shorter period (Aug. 1, 1934, to May 1, 1938), dividing all autopsies into age groups, and indicating the *actual* autopsy incidence of the various forms of cardiovascular disease, fatal and nonfatal. In the previous paper it was possible only to indicate the *relative* incidence of the etiologic types of heart disease.

For this study, 877 consecutive autopsies performed by members of the staff of the Department of Pathology of the Medical College of the State of South Carolina were reviewed. Most of the cases were from the charity services of the Roper Hospital, which is a general county hospital for both white and negro patients. All medical examiner's cases occurring in Charleston County during the period were also included.

In the total group there were 700 negroes (79.8 per cent) and 177 whites (20.2 per cent), and 540 males (61.6 per cent) and 337 females (38.4 per cent). Two hundred forty of the total number of autopsies, or 27.3 per cent, were done on persons 20 years of age, or younger.

The criteria used for the diagnosis of cardiovascular diseases were the same as those employed in our previous study.[1] The complete classification which was used is as follows:

1. Congenital cardiovascular disease
   (1) Discovered incidentally at autopsy—5 cases
   (2) Fatal—2 cases
2. Hypertensive cardiovascular disease
   (1) Incidental discovery of satisfactory evidence of hypertension —19 cases
   (2) With congestive heart failure—35 cases
   (3) With azotemia—32 cases
   (4) With uremia and edema—5 cases
   (5) With coronary thrombosis and heart failure—2 cases
   (6) With cerebral hemorrhage with or without thrombosis—26 cases

*This work was begun while the authors were at the Medical College of the State of South Carolina, the former in the Department of Pathology, and the latter as an undergraduate.

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(7) With thrombotic gangrene (extremity, mesentery, etc.)—3 cases
(8) With other vascular disease and heart failure—4 cases

3. Atherosclerosis (without hypertension)
   (1) Generalized arteriosclerosis (not hypertension) as cause of death—14 cases
   (2) Fatal coronary thrombosis without hypertension—9 cases
   (3) Other vascular accident without hypertension—18 cases
4. Syphilitic cardiovascular disease
   (1) Incidental discovery of uncomplicated syphilitic aortitis—56 cases
   (2) Incidental discovery of syphilitic aneurysm (any vessel)—6 cases
   (3) Incidental discovery of syphilitic aortic valvulitis—11 cases
   (4) Syphilitic valvulitis of aortic valve, with heart failure—15 cases
   (5) Narrowing or occlusion of coronary ostia by syphilitic plaques—10 cases
   (6) Fatal syphilitic aneurysm of any vessel—14 cases
   (7) Syphilitic myocarditis—3 cases
5. Rheumatic heart disease.
   (1) Incidental discovery of evidence of previous rheumatic heart disease—3 cases
   (2) Death from active rheumatic carditis—1 case
   (3) Sequelae of rheumatic heart disease, with heart failure—4 cases
6. "Inflammatory" diseases of the heart
   (1) Acute bacterial endocarditis—5 cases
   (2) Subacute bacterial endocarditis—3 cases
   (3) Acute myocarditis—2 cases
   (4) Tuberculous pericarditis—7 cases
   (5) Acute pericarditis, nonrheumatic and nontuberculous—18 cases
   (6) Adhesive pericarditis—2 cases
7. Chronic pulmonary disease resulting in heart failure—5 cases
8. Beriberi—3 cases

No classification is provided for incidental atherosclerosis which was not a cause of death. This was not included because of the difficulty of evaluating the personal factor in the autopsy protocols and of determining the actual amount of atherosclerosis in a given case.

CARDIOVASCULAR DEATHS IN GENERAL

It is common knowledge that the incidence of cardiovascular disease as a cause of death increases in the later years of life. This fact is shown graphically in Chart 1, in which the incidence of cardiovascular disease

in each decade is expressed as the percentage of all autopsies in that decade. After the age of 30, cardiovascular disease was the cause of death in over 40 per cent of the cases, and in an additional 13 to 27 per cent there was evidence of cardiovascular disease at autopsy, but death was caused by some other condition. After the age of 70, there was evidence of vascular disease in all cases, and in more than three-fourths of the instances vascular disease was the cause of death.

On the other hand, the incidence of death from heart failure proper (Nos. 1 (2), 2 (2), 2 (4), 2 (5), 2 (8), 3 (2), 4 (4), 4 (5), 4 (7), 5 (2), 5 (3), 6 (6), 7, and 8) does not show this progressive rise throughout the decades. In Chart 2 the deaths from cardiovascular disease are divided, separating cases of heart failure (including coronary thrombosis) from cases in which death was a result of vascular accidents (chiefly cerebral hemorrhage or thrombosis). The proportion of patients who died from heart failure rises to a peak of 22.8 per cent of all autopsies in the sixth decade, and then rapidly falls after that period. Vascular accidents

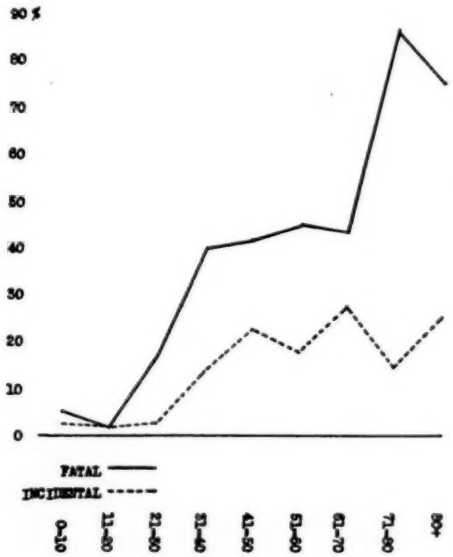

Chart 1.—Incidence of cardiovascular disease in 877 autopsy cases, by age groups (age at death).

reach an early peak in the sixth decade (when the incidence of hypertension is high) and then climb steadily after the age of 70. (The discrepancy between Charts 1 and 2 is caused by the exclusion from Chart 2 of patients who died of generalized arteriosclerosis, without heart failure or vascular accident.)

In Chart 3 the incidence of cardiovascular disease in different race and sex groups is compared. In 43.9 per cent of the autopsies on negro males there was evidence of cardiovascular disease, and, in 28.7

per cent, death resulted from the vascular disease. The incidence of cardiovascular disease and the death rate from cardiovascular disease are significantly lower in the other groups. (These figures represent patients of all ages, not just adults.)

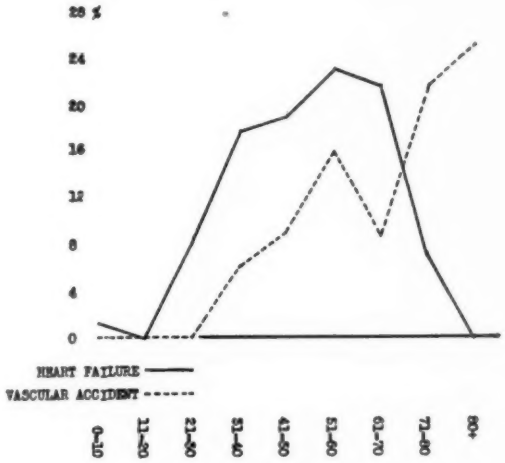

Chart 2.—Incidence of congestive heart failure and of vascular accidents in 877 autopsy cases, by age groups (age at death).

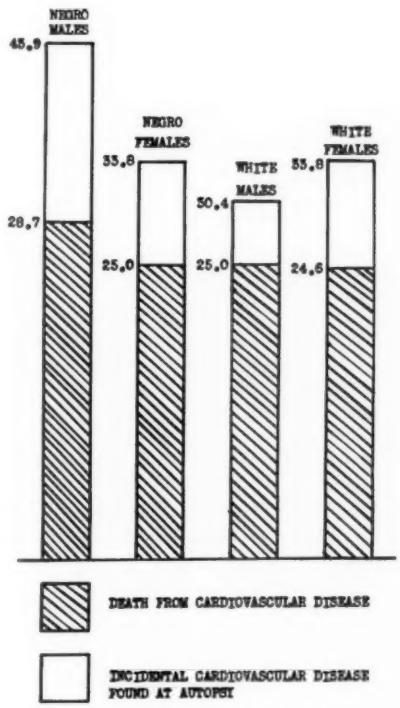

Chart 3.—Incidence of cardiovascular diseases in all autopsy cases, by race and sex.

HYPERTENSIVE CARDIOVASCULAR DISEASE

No attempt is made in this presentation to differentiate between "essential hypertension" and the hypertension of chronic glomerulonephritis.

We have adopted a combined clinical and necropsy viewpoint in making this diagnosis post mortem, requiring two of the three following factors in each case:

1. Evidence of hypertension during life (diastolic pressure of 100, or above, or a systolic pressure of 160, or above, provided the diastolic pressure is not below 70).
2. Cardiac hypertrophy without valvular lesions (more than 500 Gm.).
3. Contracted kidneys (125 Gm., or less), with microscopic evidence of arteriolar sclerosis.

On the basis of these criteria, hypertensive cardiovascular disease was the most common vascular disease encountered in the series (129 cases). In 110 cases, death was thought to be caused by hypertension and its effects, viz., heart failure, uremia, or vascular accident. In nineteen cases, death was apparently unrelated to the hypertension.

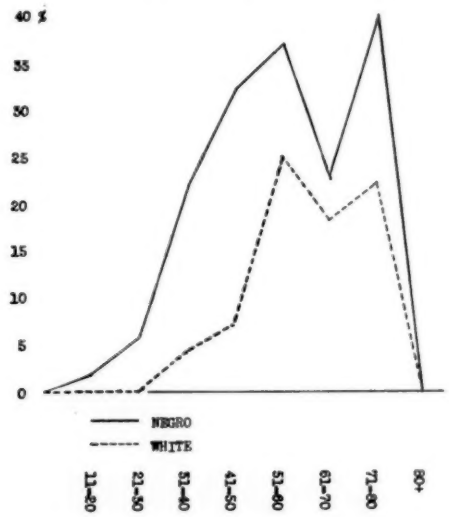

Chart 4.—Incidence of hypertensive disease in all autopsy cases, by race and age (age at death).

In Chart 4 the incidence of hypertensive vascular disease in each decade is expressed as the percentage of all autopsies in that decade. In both the white and negro races there was a fall in the incidence of the disease in the seventh decade, with peaks in the sixth and eighth decades. In the negro, the incidence of hypertension is appreciably higher than in the white throughout life, especially in the fifth decade.

In Chart 5 the incidence of hypertensive disease in the two sexes is compared by age groups. Its incidence increases about equally in

the two sexes, but the crest of the curve is flatter in the females than in the males, indicating that after the age of 30 the disease occurs about equally in the subsequent decades.

In each of the curves shown in Charts 4 and 5 it is seen that a sharp rise occurs, reaching a peak at about 51-60, which is followed by a

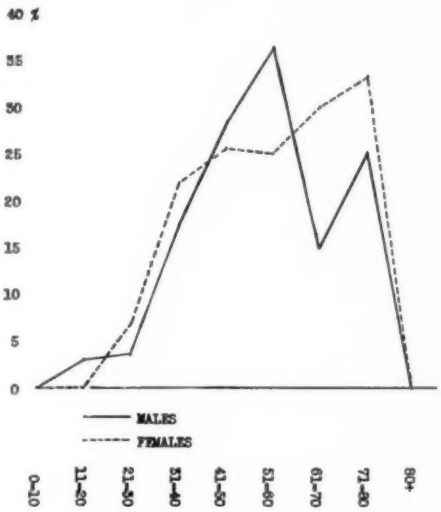

Chart 5.—Incidence of hypertensive disease in all autopsy cases, by sex and age (age at death).

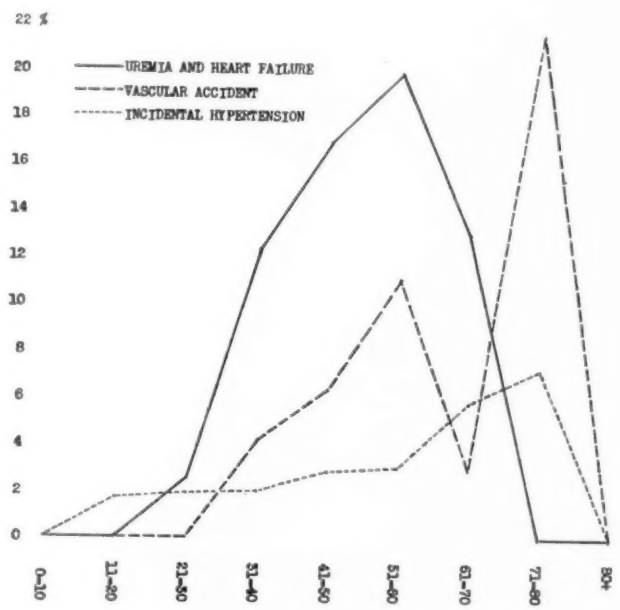

Chart 6.—Incidence of various forms of hypertensive disease in all autopsy cases, by age groups (age at death).

fall, and then by a rise between the ages of 71 and 80. The second peak is caused by a great relative increase in the number of vascular accidents associated with hypertension in the eighth decade, as shown in Chart 6. Deaths from uremia and heart failure follow a rather smooth curve, reaching a peak in the sixth decade and subsequently falling. More than one-third of all patients autopsied during this decade of life (51-60) showed evidence of hypertension, and 30.7 per cent of all patients autopsied during this decade died as a result of hypertension. The high incidence of hypertension at this period probably accounts for the increase of vascular accidents during that decade, and an increase in degenerative vascular changes in later life doubtless accounts for the second peak shown in the curve of Chart 6.

The actual number of patients who died from any cause in the later decades was, of course, small, but the proportion of vascular accidents among them was very high. In the negroes, apoplexy occurred much earlier in life than in the whites.

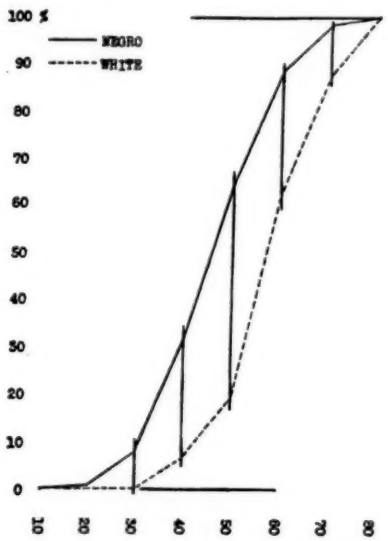

Chart 7.—Cumulative graph of hypertension, showing percentage of all deaths from hypertension (abscissae) occurring before various ages (ordinates).

In Chart 7, the distribution of cases of hypertension through the decades (age at death) in the two races is shown and is expressed in a cumulative manner. Death from hypertension occurs much earlier in the negro than in the white. Among the negroes in this series, 64.6 per cent of all patients with hypertension died before the age of 51; among the whites, 18.8 per cent died before attaining the age of 51. Among the negroes, 31.9 per cent of the patients with hypertension died before the age of 41; among the whites, only 6.3 per cent died before attaining the age of 41.

SYPHILITIC CARDIOVASCULAR DISEASE

A very common organic change found in the cardiovascular system at autopsy is syphilitic aortitis; it was found in 108 cases in this series (12.3 per cent) (Chart 8). Of all negro males who died between the ages of 31-40, 36.7 per cent showed evidence of syphilitic aortitis. Of all of the patients with aortitis, fifty-two, or 48.1 per cent, showed, in addition, one or more of the following complications of syphilitic aortitis: aneurysm, narrowing of the coronary ostia, or valvulitis of the aortic valve, with insufficiency. The other fifty-six patients (51.8 per cent) had uncomplicated syphilitic aortitis, but one of these died of syphilitic myocarditis.

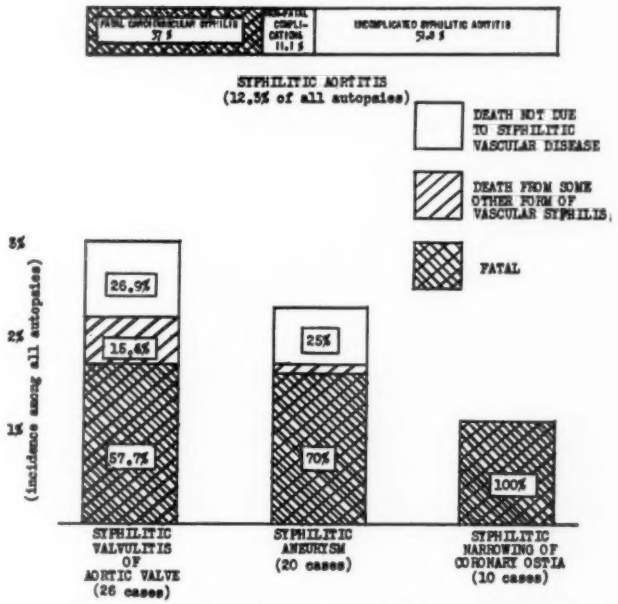

Chart 8.—Incidence of various forms of syphilitic cardiovascular disease.

Syphilitic valvulitis of the aortic valve was found in twenty-six cases (3 per cent of the entire autopsy group), but in only fifteen cases was the valvular insufficiency, per se, thought to be the cause of death. Four additional patients died of cardiovascular syphilis; three of these apparently died as a result of narrowing or occlusion of the coronary ostia by syphilitic plaques, and one died of aneurysm. One patient died of subacute bacterial endocarditis, implanted on the damaged aortic valves. Six patients with insufficiency of the aortic valve caused by syphilis died of some other, entirely unrelated, condition, usually an infectious process.

Twenty cases of syphilitic aneurysm were encountered (2.3 per cent of the whole series of autopsies), and in fourteen of these, death was a result of the aneurysm, usually from rupture and hemorrhage, occa-

sionally from compression of vital structures. In two cases insufficiency of the aortic valve caused by syphilis was also present, and in one of these cases the patient died of congestive failure. In the other five cases, death was in no way related to cardiovascular syphilis.

In all of the cases in which there was syphilitic narrowing of the ostia of the coronary arteries, death was more or less arbitrarily assigned to that lesion, even if other evidences of cardiovascular syphilis were also present. Three of the ten patients in this group also had syphilitic insufficiency of the aortic valve. In most instances in which occlusion of the coronary ostia by syphilitic aortic plaques was noted, death occurred rather suddenly, during exertion and without the usual manifestations of congestive heart failure.

There was evidence of syphilitic cardiovascular disease in 14.6 per cent of all negroes, and in 5.6 per cent of the whites, who came to autopsy during the period studied. Twenty-one negroes who showed evidence of syphilitic aortitis died of hypertensive disease.

CORONARY THROMBOSIS

Coronary thrombosis, either with or without hypertension, is of relatively rare occurrence in the negro. Only five of the 700 negroes in this series showed evidence of coronary thrombosis, comprising 1.4 per cent of all autopsies on negroes who died after the age of 30. In the whites, coronary thrombosis was about four times as common; it was the cause of death in 5.3 per cent of all patients over 30, and it occurred six times among 177 whites. In the whites, coronary thrombosis comprised 14.6 per cent of all fatal cases of cardiovascular disease after the age of 30; in the negroes, it made up only 3.0 per cent of the cases of fatal cardiovascular disease after the age of 30. When coronary thrombosis occurred in persons who showed evidence of hypertension, the average age at death was 35; when it occurred in persons who had no evidence of hypertension, the average age at death was 62.

OTHER FORMS OF VASCULAR DISEASE

Arteriosclerosis (without evidence of hypertension) was more commonly a cause of death in the white than in the negro patient in this series. Among the whites, 14.9 per cent of all autopsies after the age of 30 showed that death was the result of arteriosclerosis (frequently vascular accident), without evidence of hypertension. In the negroes, 6.6 per cent of all autopsies after the age of 30 showed that death was caused by arteriosclerosis. Arteriosclerosis without hypertension was the cause of death in 41.5 per cent of all cases of fatal cardiovascular disease after the age of 30 in the whites, and in 14.5 per cent in the negroes.

In this series of cases only five deaths occurred as a result of rheumatic heart disease (active or inactive). Four of these were in negroes. The

age at death ranged from 22 to 65 years. Three additional patients showed evidence of previous rheumatic infection of the heart at autopsy, but they did not die of rheumatic heart disease. Of all cases of fatal cardiovascular disease in the negro, rheumatic heart disease comprised only 2 per cent, and, in the white, 2.3 per cent.

Other types of cardiovascular disease were of even rarer occurrence.

SUMMARY

In a series of 877 autopsies performed in Charleston, S. C. from Aug. 1, 1934, to May 1, 1938, 344 patients showed evidence of cardiovascular disease, and in 243 instances this was the cause of death. Of the various etiologic types, hypertensive cardiovascular disease was the most frequently encountered, and syphilitic cardiovascular disease was next. Both of these types were much more frequent among negroes than among whites. Of all of the patients who showed autopsy evidence of hypertension, 85.3 per cent died as a result of hypertension or of conditions thought to be sequelae of hypertension. Of all of the patients who showed evidence of vascular syphilis, only 37 per cent died as a result of that condition.*

Cardiovascular disease occurred more commonly in the negro males than in any other group in this series, and likewise was more commonly the cause of death in this group than in any other.

Hypertensive cardiovascular disease occurred much earlier in life in negroes than in whites, and also occurred more frequently in negroes than in whites. In the negroes, 64.6 per cent of the patients with hypertension died before the age of 51, but only 18.8 per cent of the whites died before that age.

Syphilitic cardiovascular disease (usually syphilitic aortitis) was very common among the negroes in this series, occurring in 14.6 per cent of all autopsies on negroes, regardless of age, and in 36.7 per cent of those dying between the ages of 31 and 40.

Coronary thrombosis occurred about four times as frequently in the white as in the negro group; in the whites it comprised 14.6 per cent of all cases of fatal cardiovascular disease after the age of 30.

Arteriosclerosis was more commonly a cause of death among the whites than among the negroes, possibly because the negro, on the average, died earlier than did the white man.

Rheumatic heart disease occurred quite rarely in this series; it was found in less than 1 per cent of all cases and caused death in only 0.6 per cent of all cases.

REFERENCE

1. Peery, T. M., and Langsam, S. M.: Fatal Cardiovascular Disease in Charleston, S. C., With Particular Reference to Hypertension, Arch. Int. Med. 64: 971, 1939.

*These figures could not be transferred to living patients without serious error.

HEMOPHILUS PARA-INFLUENZAE ENDOCARDITIS

A Report of Two Cases and a Review of the Literature of the Influenzal Endocarditides

Erle B. Craven, Jr., M.D., Lexington, N. C., Mary A. Poston, M.A., and Edward S. Orgain, M.D., Durham, N. C.

SINCE the discovery by Pfeiffer,[1] in 1893, of *B. influenzae*, instances of bacterial endocarditis caused by organisms of the influenza group have been reported periodically.

It is the purpose of this paper to attempt a critical review of these reports in the light of more recent bacteriologic studies of the *H. influenzae* group, and to present two new cases of subacute bacterial endocarditis caused by *H. para-influenzae* (Rivers, 1922).

REPORT OF CASES

Case 1.—W. F. V., Jr., a white man, 40 years of age, complained of having had a low-grade fever, generalized aching, severe headache, and occasional attacks of high fever, with chills, for five months.

The family history was irrelevant, and, except for influenza in 1919, followed by a slow convalescence lasting several months, the past history was unimportant.

The present illness began abruptly in April, 1937, with sore throat, fever, headache, and generalized aching. These symptoms continued without appreciable change, except for chills and higher fever at widely separated intervals, until Nov. 4, 1937, when the patient became acutely ill, with higher fever and more severe pain, accentuated by movement, in the suboccipital and posterior cervical regions.

On physical examination (Nov. 11), the patient was found to be undernourished, febrile, obviously acutely ill, and suffering extreme discomfort. The temperature was 39° C., the pulse rate 80, the respiratory rate 20, and the blood pressure 112/72. The neck was slightly hyperextended, and resisted flexion, which was extremely painful. The skin was hot, dry, and slightly scaly. The mucous membranes were pale. There were no petechiae or rashes. The pupils were normal in size and shape and reacted normally to light and during accommodation. Ophthalmoscopic examination revealed slightly hazy optic discs. The retinal arterioles appeared normal. There was nothing remarkable about the nose, ears, mouth, and throat. The heart was enlarged to the left, with the apical impulse visible and palpable in the fifth intercostal space, 11 cm. from the midsternal line. The first sound at the apex was diminished in intensity, and was followed by a rough, blowing, systolic murmur which was transmitted into the axilla. The aortic and pulmonic second sounds were normal, and no diastolic murmurs were heard. The radial pulses were slow and soft. The abdomen was scaphoid. There was an area of moderate tenderness to deep pressure over the sigmoid colon, but no masses were felt. The liver, spleen, and kidneys were not palpable. Rectal examination disclosed no abnormalities. The reflexes were physiologic. There was no ankle clonus, and the Babinski and Kernig signs were negative. Examination of the cranial nerves elicited normal responses, and the motor and sensory systems were intact.

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Examination of the blood showed that the hemoglobin was 68 per cent (Sahli), the erythrocyte count 4,200,000, the erythrocyte volume 35 per cent, and the leucocyte count 14,000. The differential count showed 78 per cent polymorphonuclear leucocytes, 14 per cent small lymphocytes, 4 per cent large lymphocytes, and 4 per cent mononuclear cells. There were no abnormal cells or parasites in the stained smear. A voided specimen of urine showed a few leucocytes, but no albumin, sugar, or casts.

The spinal fluid pressure, which was initially 160 millimeters of spinal fluid, reacted normally to jugular compression. The fluid was slightly turbid and contained a few small shreds of fibrin; it contained 84 cells per c.mm., 80 per cent of which were mononuclear, and 20 per cent polymorphonuclear, cells. No organisms were found in the stained, centrifuged sediment, and cultures in blood broth remained sterile. Guinea pig inoculation revealed nothing abnormal. Blood cultures which were made Nov. 11 and Nov. 13 were sterile after twenty-five days.

The spinal puncture, which was repeated Nov. 17, yielded a cloudy fluid containing many strings of fibrin and 1,475 cells per. c.mm., of which 91 per cent were polymorphonuclear leucocytes and 9 per cent lymphocytes. In the stained smear a few, small, Gram-negative coccoid forms were seen, but the organisms did not grow in broth enriched with erythrocytes and serum.

A provisional diagnosis of chronic meningococcus septicemia and meningitis was made, and the patient was given antimeningococcic serum, both intrathecally and intramuscularly, together with maximal therapeutic doses of sulfanilamide by mouth for two weeks. Spinal punctures were done daily, and after an initial rise of the cell count to 7,600, 100 per cent of which were lymphocytes, the counts slowly fell until, on Dec. 18, there were only 42 cells, all of which were lymphocytes. From Nov. 20 to Nov. 23 the temperature slowly subsided, and all signs of meningeal irritation disappeared. Severe serum sickness began Nov. 23; it was accompanied by a chill and a fever which persisted until Nov. 30, after which the patient was afebrile for four days. Clinically, improvement during this time was evident but not striking. A low-grade fever, reaching 38.8° C., recurred Dec. 4, and on Dec. 7 a second course of sulfanilamide was begun. The temperature fell to normal on Dec. 8, and did not rise again above 37° C. for nine days. During this 9-day period the patient appeared and felt remarkably improved. With increase of appetite and gain in weight, he insisted upon sitting up in a chair several times each day. However, following the discontinuance of sulfanilamide, Dec. 18, the fever recurred, ranging between 38° C. and 38.5° C.

Blood cultures taken on Dec. 29, 1937, and Jan. 24, 1938, were positive for *H. para-influenzae*. An autogenous vaccine prepared from the cultures was given in graduated doses intravenously without any apparent effect.

On Jan. 30, 1938, the patient was transferred to Duke Hospital, where, in spite of numerous blood transfusions and the readministration of sulfanilamide in doses sufficient to give a blood concentration of 13 mg. per cent, he became progressively worse. During the last weeks of his illness the systolic murmur at the apex became louder and harsher, and a presystolic murmur appeared. Crops of bright red petechiae appeared nearly every day in the skin and mucous membranes, and urinary abnormalities simulating those of acute glomerulonephritis indicated embolism of the kidneys. The liver and spleen became greatly enlarged. On Feb. 7, because of severe pain in the left upper quadrant of the abdomen and in the lower portion of the chest, splenic infarction was suspected. The patient became semicomatose on March 1, and died rather suddenly on March 10, approximately 330 days after the onset of his illness.

The necropsy was performed by Dr. W. C. Sealy. The body was that of a well-developed but poorly nourished white man, about 40 years of age, measuring 185 cm. in length. Numerous purplish petechiae were scattered over the entire body, par-

ticularly in the skin over the thorax and arms. Over the left heel, involving part of the plantar surface of the foot, there was a large, purplish, discolored area, measuring about 5 cm. in diameter. A similar area was present over the right external ear.

Abdominal Cavity.—The peritoneal surfaces were smooth, and no free fluid was present within the cavity. The spleen was quite large, weighing 550 grams; the capsule was smooth and free of adhesion. Numerous infarcts, varying in size, color, and age, were present throughout the spleen, and there was one area of necrosis from which purulent material was expressed. On section, the splenic pulp bulged, and the Malpighian bodies were easily made out. Microscopic section showed many infarcts, old and new. Some had thick fibrous walls surrounding caseous centers. Others contained degenerating splenic pulp and large areas of hemorrhage. Small miliary abscesses were present througout the sections. Marked infiltration of the spleen with polymorphonuclear leucocytes was also present. Specially stained sections showed no bacteria.

The stomach and duodenum were normal except for a few, scattered, mucosal petechiae. Throughout the entire length of the small and large intestines there were many petechiae, but no other abnormalities were noted.

The liver was large, weighing 2,095 grams. It was normal except for a few, small, widely separated scars. Microscopically, a moderate degree of fatty degeneration, particularly around the central veins, was found.

The left kidney weighed 330 grams; its capsule stripped with ease except over an area of old infarction. The underlying kidney substance contained numerous infarcts varying in size and age from petechiae to old white scars. The pelvis and ureter showed nothing but fairly numerous petechiae in the mucous membrane. The right kidney weighed 180 grams, and had a double pelvis and ureter, which exhibited no dilatation or obstruction. Innumerable areas of infarction were present.

Microscopic sections revealed a minimal cellular response, predominantly mononuclear in type, with some fibroblastic proliferation, and, in one recently infarcted area, hyalinization of the tubules and glomeruli was present.

The bladder was dilated, its wall was thin, and its mucosa was normal except for scattered petechiae.

Thoracic Cavity.—The left lung weighed 350 gm.; it and the left pleura were normal. The right lung weighed 450 grams. Fairly dense and extensive adhesions extending from the upper lobe to the parietal pleura were present. The apex was definitely nodular to palpation, and, on section, several small, healed tubercules were seen. No areas of consolidation or atelectasis were evident in either lung. Microscopic sections showed only some congestion at the bases of the lungs, and one small area of consolidation composed largely of leucocytes.

Pericardial Cavity.—The pericardial surface was thin, smooth, and glistening. No free fluid was present. The heart weighed 300 grams. The epicardium was smooth throughout. The larger vessels opened into the heart in the normal manner, and there were no emboli in any of these vessels. The endocardium was perfectly smooth. The right ventricle was beefy-red in color. The chamber was slightly dilated, the wall measuring 0.2 cm. in thickness. The left ventricular wall, similarly red, measured 1.5 cm. in thickness. No dilatation was present. Throughout the myocardium numerous small areas of scarring, some quite fresh, were found. The aortic, pulmonic, and tricuspid valves appeared normal. The valve measurements were as follows: aortic, 7.5 cm.; mitral, 10 cm.; pulmonic, 6.5 cm.; tricuspid, 12 cm. On the anterior cusp of the mitral valve there was a large vegetation, measuring 3 by 4 by 2 cm., which was papillomatous in appearance and extended well into the cavity of the left auricle. It was light brown in color, nonfriable, and firmly attached to the underlying valve. The remaining portion of the valve showed no scarring or ulceration, and the posterior cusp

was normal. The chordae tendineae were normal. The coronary vessels were patent throughout, and showed no arteriosclerosis. The aorta was normal.

The microscopic sections showed no increase in fibrous tissue; the nuclei were prominent, and the muscle bundles were normal in size. However, in some sections, there were numerous miliary abscesses characterized by polymorphonuclear leucocytic infiltration. The epicardium was normal throughout. The endocardium over the lower portion of the heart was thin and normal in appearance, but as the base was approached numerous small vegetations were encountered. Some of them were covered with endothelium, but the bulk of the vegetation was composed of fibrin, polymorphonuclear leucocytes, and fibroblasts; very few newly formed blood vessels could be seen. Other vegetations were ulcerated completely; this was true of the vegetation on the mitral valve itself. A large amount of fibrin and necrotic debris was present in the ulceration. The base of the ulceration was composed of many fibroblasts, newly formed blood vessels, and leucocytes. The myocardium just beneath the ulceration was infiltrated with mononuclear cells and leucocytes. The muscle fibers in this region showed some degeneration. The mitral valve, except for its base, was composed entirely of the large vegetation described grossly. The base of the valve was thin, and showed no inflammation, but the free edge was composed entirely of the large ulcerating mass described above.

Cranial Cavity.—The venous sinuses were patent. Beneath the arachnoid, yellowish areas and small petechiae could be seen over the brain substance. Two large areas of hemorrhage into the brain substance were also present. The cerebrospinal fluid was straw-colored and nonpurulent. The spinal cord was not examined. Microscopic sections through the cerebrum at the level of the superior colliculus showed a marked leptomeningitis, characterized by thickening of the meninges and moderate infiltration with leucocytes and round cells. The underlying brain tissue was involved in several areas. In one section there was a superficial abscess that involved the cortex. It had a well-defined fibrous tissue wall, and the leptomeninges walled it off completely from the subarachnoid space. The abscess was composed largely of necrotic brain tissue.

Anatomic Diagnoses.—Acute and chronic meningitis *(H. para-influenzae);* subacute vegetative endocarditis *(H. para-influenzae),* with verrucous vegetation and mycotic aneurysm in the mitral valve and auricular wall; subacute glomerular nephritis and interstitial nephritis; multiple infected infarcts in spleen and kidneys; multiple abscesses in spleen and myocardium; multiple mycotic aneurysms of cerebral arteries; multiple petechiae in the skin and mucous membranes; acute splenic tumor; dilatation of the right ventricle; slight passive congestion of liver; pulmonary emphysema; double pelvis and ureter on the right side.

CASE 2.—E. C., a 15-year-old negro school girl, entered Duke Hospital March 10, 1938, complaining of chills and fever of three and one-half months' duration.

The family history was irrelevant, and, except for measles, her general health had always been excellent. She specifically denied having had rheumatic fever, chorea, tonsillitis, or frequent upper respiratory infections.

The present illness began during the first part of December, 1937, three and one-half months prior to her admission, when she developed generalized muscular aching which was quickly followed by a chill and high fever. During the next two weeks she had four similar attacks, and, because of continued general malaise and fever, she was withdrawn from school to remain at rest at home, but was not confined to bed. In January, 1938, two months after the onset, a physician was consulted because of pain in the left chest, anteriorly, which radiated into the left upper abdominal quadrant, and made a diagnosis of pneumonia. She recovered after one week of rest in bed, but chills, fever, and pain in both sides of the chest, without cough,

recurred several times in the ensuing thirty days. Six weeks before entry, during one of these attacks, a diagnosis of pneumonia was again made; at this time her temperature ranged from 39.4° to 41° C. After three weeks of rest in bed, the patient was allowed to be up, but was quickly forced to go back to bed again because of weakness and anemia. During the three weeks prior to entry she apparently improved, and was free of chills, but developed a nonproductive cough. On the day of admission there was a severe chill, with a fever of 40° C. She had no sputum, hemoptysis, or night sweats. The patient felt that she had lost weight, but could not estimate the amount.

Physical examination revealed a well-developed, fairly well-nourished, oriented, cooperative negro girl, who, in spite of the degree of elevation of her temperature, did not appear acutely ill. Her temperature was 40.6° C., her pulse rate, 150, and her respiratory rate, 36. Skeletal examination revealed no abnormalities. Small, firm, nontender lymph nodes were palpable in the cervical, axillary, and inguinal regions, bilaterally. The mucous membranes were pale; no petechiae were seen. The pupils were equal and regular in outline, and reacted well to light and during accommodation. The optic fundi were normal. The ears and nose showed no abnormalities. The teeth were clean and in good repair. The tongue was coated. The tonsils were enlarged and cryptous; the pharynx was normal. The cervical veins were not engorged. The respirations were rapid and shallow. A friction rub was felt over the left chest anteriorly. Over the left lower lobe, posteriorly, there was dullness to percussion; the breath sounds were diminished in intensity without change in pitch; no râles were heard. Friction rubs were audible over the anterior and axillary regions of both chests, and posteriorly over the right lower lobe. The heart was enlarged moderately to the left, with a diffuse apical impulse, maximal in the fifth intercostal space. The left border of dullness was 9.5 cm. from the midsternal line. Systolic and diastolic thrills were present in the left third and fourth intercostal spaces. A soft systolic murmur and a faint protodiastolic gallop rhythm were audible at the apex. Over the pulmonic area a blowing systolic murmur was heard; the pulmonic second sound was accentuated, and was followed by a harsh diastolic murmur which was transmitted down the sternum to the fourth intercostal space. The aortic second sound was not accentuated. The rate was 150 beats per minute, and the rhythm was normal. The radial pulse was soft and collapsing in type, and the blood pressure was 125/45. The liver was felt just below the right costal margin. Slight tenderness to deep palpation was present in the left flank. The spleen and kidneys were not felt. Pelvic examination revealed a mucopurulent vaginal discharge. Rectal examination was negative. The extremities were grossly normal, and the reflexes were physiologic.

Examination of the blood showed that the hemoglobin was 4.3 grams (27 per cent), the erythrocyte count, 1,720,000, and the leucocyte count, 32,480. The erythrocytes showed anisocytosis, poikilocytosis, and central achromia. The differential count showed 89 per cent polymorphonuclear neutrophils; 1 per cent eosinophils; 1 per cent monocytes; 3 per cent large lymphocytes; and 6 per cent small lymphocytes. The blood Wassermann and Kahn reactions were strongly positive (4 plus) on four occasions. A catheterized specimen of urine contained a few erythrocytes and 8 leucocytes per high-power field, and gave a faintly positive benzidine reaction, but contained no sugar or albumin. Repeated examination of the urine revealed variations in specific gravity from 1.006 to 1.028, occasional traces of albumin, and many erythrocytes. The nonprotein nitrogen content of the blood was 26 mg. per cent. The gonococcal complement fixation test was negative. A sputum culture showed *Alpha hemolytic streptococcus, Staphylococcus aureus,* and *Pharyngis siccus.* The electrocardiogram revealed sinoauricular tachycardia, with a rate of 145, a P-R interval of 0.12 sec., a QRS interval of 0.07 sec., an inverted T_1, a diphasic T_2, an upright T_3, and an inverted T_4. The T-wave abnormalities sug-

gested definite myocardial injury. A roentgenogram of the lungs showed irregular mottling in the mid-portion of the right lung and in the left lower lobe, suggesting pneumonitis. A blood culture revealed less than one colony of *H. para-influenzae* (nonhemolytic) per cubic centimeter; tests for bacteriolysins and opsonins were negative; agglutinins were present in a serum dilution of 1:80.

During the first week in the hospital, the fever persisted at a level of 39 to 40° C.; the pulse rate varied from 120 to 130, and was uninfluenced by complete digitalization. The patient was quite comfortable except for pleuritic pain, which ceased when the friction rubs disappeared. The leucocyte count varied between 12,000 and 32,000, and three blood cultures were negative. By the seventh day the temperature fell to 38, but during the ensuing two weeks rose in wide daily swings to 39 or 40.5° C. In the midst of this febrile period, five consecutive blood cultures were positive for *H. para-influenzae*. There was little general change in her condition, but she continued to have transient, mild to severe, pain in both sides of the chest, with cough productive of small amounts of mucoid sputum, but no blood. Râles persisted fleetingly in both lower lobes, and the basal pulmonic murmurs became louder. Repeated transfusions raised the hemoglobin to 6.6 grams and the erythrocyte count to 3,240,000. On the eighteenth hospital day the administration of sodium disulfanilamide was begun. The following day she became afebrile and remained so for nine days, during which time she improved to the point of being symptom-free; the intensity of the heart murmurs decreased definitely; the leucocyte count fell until it ranged from 9,000 to 14,000 cells per cu. mm., and two blood cultures were negative. Thereafter, for the remaining twelve days before death, her temperature ran in sharp peaks to 39° C., or above; the leucocyte count rose to 20,000; the pulmonic murmurs increased greatly in intensity; the pain in her left chest reappeared; and two blood cultures were positive for the same organism. During the last week in the hospital, she received six injections (approximately 100 c.c. each) of anti-influenza serum which agglutinated the patient's organism in a dilution of 1:1,280, and inhibited its growth in a dilution of 1:200. Severe reactions, in the form of chills and fever, attended each injection except the final one. In the last twenty-four hours she became acidotic and almost anuric. Because of a CO_2 combining power of 36 vol. per cent, 500 c.c. of ⅙ molar lactate were given slowly intravenously, without improvement. The patient became comatose and went into shock, and the usual symptomatic measures were entirely ineffective. Death occurred on April 20, 1938, forty days after admission and approximately 120 days after the onset of her illness.

The necropsy was performed by Dr. Phillip Parsons. The body was that of a well-developed, but slender, negress, measuring 155 cm. over all.

Abdominal Cavity.—No free fluid or evidence of peritonitis was found. The liver, intestines, and pelvic viscera appeared normal. The spleen was slightly enlarged, weighing 300 grams; its capsule was smooth, and free from evidence of inflammatory lesions or infarcts. On section, the pulp was smooth, dull, red, and homogenous. The microscopic appearance was that of acute splenic tumor. The liver weighed 1,400 grams, and showed only a few, small, reddish areas beneath the capsule. Microscopic sections revealed multiple foci of necrosis, with accumulations of leucocytes. The stomach, duodenum, and adrenals were normal. The right kidney weighed 200 grams, and was greatly swollen. The capsule stripped easily; beneath the capsular surface there were numerous punctate, hemorrhagic spots. The pelvis was normal. The left kidney weighed 200 grams and was similarly involved.

Microscopic section showed unusual proliferation of the supporting tissue of the glomeruli, manifested by an extraordinary number of nuclei. The tubules contained masses of blood. The tubular epithelium appeared swollen, but there was little hyalin formation.

Thoracic Cavity.—The left pleural space was obliterated by an inflammatory process, with dense, fibrous adhesions between lung and parietal pleura. The left lung weighed 400 grams. The pleural surface was roughened, with many fibrous tags. Palpation revealed numerous areas of firm consolidation which, when sectioned, appeared as sharply circumscribed, dark-red areas of infarction. The bronchi showed no obstruction. The right pleural space was similarly obliterated by dense fibrous adhesions. The right lung weighed 420 grams. Multiple areas of infarction, like those found on the left side, were present. A large mass of caseating lymph nodes, surrounded by dense fibrous tissue, was found at the bifurcation of the major bronchus.

Microscopic sections revealed a variety of infarcts, consisting of fresh, hemorrhagic lesions, old, organized lesions, representing the pulmonary reaction to extensive focal destruction of pulmonary tissue, and areas with extensive central necrosis. The mediastinal lymph nodes were slightly enlarged.

Pericardial Cavity.—The pericardial sac contained 100 c.c. of clear, straw-colored fluid. The heart weighed 300 grams. The heart was enlarged, and there were dilatation and hypertrophy of the right ventricle. The endocardium and pericardium were smooth. The myocardium was firm, but on section was extremely pale. The mitral, aortic, and tricuspid valves appeared normal. The valve measurements were as follows: aortic, 5 cm.; mitral, 7 cm.; pulmonic, 7 cm.; tricuspid, 10 cm. The anterior cusp of the pulmonic valve was completely destroyed by a large mass of vegetations. The adjacent cusps showed fresh, delicate, granular lesions on the valvular surface. In the main trunk of the branch of the pulmonary artery leading to the right lung there was a huge thrombotic mass which seemed to obstruct the circulation of this lung completely. Section in the longitudinal axis disclosed the fact that the blood vessel wall was completely destroyed by an infectious process. The whole area was overlaid with thrombus. Distal to this point, the smaller vessels appeared to be diminished in size, or completely occluded, by a combination of thrombosis and endarteritis. The aorta was normal throughout its length.

Microscopically, the heart muscle was the seat of an acute, diffuse, inflammatory process, with extensive infiltration of leucocytes and wandering cells about the blood vessels and in the intermuscular septa, but without abscess formation. Section of the pulmonary valve showed an acute inflammatory process, with polymorphonuclear infiltration and fresh fibrin formation.

Anatomic Diagnoses.—Bacterial endocarditis (*H. para-influenzae*), with vegetations on the pulmonic valve; ulcerative destruction of the pulmonary valve; pulmonary insufficiency; acute, diffuse myocarditis; cardiac dilatation and hypertrophy; destruction of the left branch of pulmonary artery by an infected thrombus; multiple infarcts in lungs, fresh and old; fibrous pleural adhesions; multiple, focal necrosis of lungs; acute hemorrhagic glomerulonephritis; acute splenic tumor; cerebral petechiae.

BACTERIOLOGY

The organisms, small, Gram-negative pleomorphic rods, were grown from the blood during life in both cases. In Case 1, two out of a total of twelve cultures were positive, and, in Case 2, nine of twelve cultures were positive. That the organism is frequently quite difficult to grow during life is attested by the experience of many observers and by our experience in Case 1, in which positive cultures were obtained only when the broth was enriched by the addition of indifferent human serum. We believe, with Horder,[2] that "carefully arranged blood cultures in infective endocarditis usually yield a growth of some microbe of definite pathogenicity. The frequency with which blood

cultures are positive in this disease turns very largely upon the technique employed. When every facility is given to the microorganisms to grow in the media used, it may be said that positive cultures are obtained sooner or later in the course of the disease in 90 per cent of cases."

In Case 1, at necropsy, the organism was grown from the heart's blood, endocardial vegetations, and spleen. In Case 2, at necropsy, it was grown from the heart's blood, endocardial vegetations, spleen, and lungs.

The organisms in both cases required V factor, but not X factor, for growth. Neither organism caused hemolysis. Both produced indol and reduced nitrates. Both produced acid in dextrose, maltose, and sucrose, but not in mannite, lactose, or salicin. Neither organism was pathogenic for mice, rabbits, nor guinea pigs. The thermal death points were as follows:

	Case 1	Case 2
39° C.	20 hours	24 hours
40° C.	18 hours	20 hours
41° C.	15 hours	18 hours
41.5° C.	10 hours	11 hours
42° C.	8 hours	10 hours

DISCUSSION

Table I lists those cases which we feel fulfill reasonable requirements for inclusion in this review of bacterial endocarditis caused by the *H. influenzae* group. These criteria are (1) repeated cultivation of the organism from the blood during life, together with sufficient clinical evidence to justify the diagnosis of bacterial endocarditis, or (2) necropsy evidence of bacterial endocarditis, plus cultivation of the organism from the heart's blood or endocardial vegetation, or both.

From the original report of two cases by Jehle, in 1899,[3] to the present time, we have been able to collect thirty-six cases (including our own) of bacterial endocarditis caused by the *H. influenzae* group of organisms which satisfy our criteria. Some of the earlier cases, such as Austin's[4] and Thayer's,[5] have not been included because the etiologic diagnosis in their cases was based on morphologic and staining characteristics alone, or because insufficient clinical data were available.

Until 1923, the organism was designated as *B. influenzae* in all of the case reports, but since more recent bacteriologic studies of the influenza group have appeared, there have been reported, more and more frequently, cases of bacterial endocarditis caused by organisms similar to, but differing in important cultural respects from, the bacillus of Pfeiffer. It now seems probable that in some of the earlier cases reported as instances of *B. influenzae* endocarditis the infection was caused by these related bacilli. For this reason, we shall include a brief summary of several important bacteriologic studies of the *H. influenzae* group.

TABLE

BACTER

DATE	AUTHORS	NO. CASES SEX AGE	CLINICAL COURSE	ANTE-MORTEM BLOOD CULTURES
1899	Jehle[3]	(2) M. 40	Acute, 4 weeks	None
			No clinical record	None
1906	Horder[27]	(2) M. 31	Subacute, 4 months	*H. influenzae* group. (Para-influenza not ruled out)
		M. 13	Subacute, 3 months	*H. influenzae* group. (Para-influenza not ruled out)
1907	Horder[27]	(1) M. 50	Subacute, 4 months	*H. influenzae* group. (Para-influenza not ruled out)
1908	Smith[28]	(1) M. 45	Subacute, 3 months Fever, embolic phenomena, Large spleen; mitral disease	*H. influenzae.* (*H. para-influenzae* not excluded)
1918	Malloch and Rhea[26]	(2) M. 39	Acute, 13 days	None
		M. 44	Acute, 6 days	None
1922	Cohen and Greenberg[29]	(1) M. 45	Subacute, 36 days	*H. influenzae* group. (Para-influenza not ruled out)
1923	Miller and Branch[18]	(1) F. 12	Subacute, 51 days	Hemolytic hemophilic bacillus (''Bacillus X''—Pritchett and Stillman, 1919) *H. influenzae,* hemolytic
1924	Bensted[30]	(1) M. 25	Acute, 8 days	Cultures negative
1926	Oppenheimer[31]	(1) M. 28	Subacute, 3 months	*H. influenzae* (para-influenza not ruled out)
1927	Ninni[32]	(1) F. 30	Clinical diagnosis of endocarditis lenta; mitral stenosis and insufficiency, aortic insufficiency	Probably para-influenza on 2 occasions
1928	Russell and Fildes[21]	(1) F. 18	Subacute, 28 days	Para-influenza, nonhemolytic

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IOLOGY

POST-MORTEM BLOOD CULTURES	AUTOPSY FINDINGS
H. influenzae group (para-influenza not ruled out) from vegetations only	Abundant, soft vegetations on aortic valve.
Same as above and staphylococcus	Vegetations on aortic valve. Influenzal bronchitis.
Same as ante-mortem cultures (from vegetations)	Old rheumatic endocarditis of aortic valve; fresh vegetative and ulcerative bacterial endocarditis.
Same as ante-mortem cultures (from vegetations)	Old rheumatic mitral endocarditis; fresh vegetative and ulcerative bacterial endocarditis. Anemic infarcts of kidneys and spleen.
Not obtained	No autopsy.
No cultures. Morphology: small Gram-negative bacilli in vegetations	Verrucose endocarditis of mitral valve; pericarditis; pleural effusion; purulent peritonitis.
H. influenzae (para-influenza not ruled out) from heart's blood, vegetations, and bronchioles	Bilateral, confluent, lobular pneumonia; ? syphilitic aortitis involving aortic ring; acute vegetative (bacterial) endocarditis of aortic cusps; cardiac dilatation; chronic interstitial nephritis.
Same as above, but from vegetations only	Bilateral lobular pneumonia; old aortic endocarditis (? rheumatic); acute vegetative endocarditis of aortic and mitral valves; cardiac hypertrophy and dilatation; acute splenic tumor; chronic interstitial nephritis.
Cultures negative	Acute vegetative and ulcerative endocarditis of mitral valve and ? of aortic valve. Left ventricular hypertrophy. Infarcts of spleen and kidneys; ? acute glomerular nephritis.
None	Vegetative and verrucose mitral endocarditis; focal embolic myocarditis; dissecting aneurysm of abdominal aorta; infarcts of spleen; glomerular nephritis; acute localized meningitis; ascites; hydropericardium.
H. influenzae group (para-influenza not ruled out) from heart's blood, vegetations, spleen, and pleural fluid	Capillary bronchitis, ? lobular pneumonia, pleural effusions; vegetative and ulcerative endocarditis of mitral valve; cardiac hypertrophy and dilatation. Purulent meningitis.
Cultures negative	Old chronic endocarditis (? rheumatic) of aortic and mitral valves; fresh vegetative bacterial endocarditis of aortic and mitral valves; cardiac dilatation and hypertrophy; ascites and hydrothorax; acute splenic tumor and infarcts; acute glomerulonephritis.
Data not available	Data not available.
Same organism from vegetations on heart valves	Old rheumatic endocarditis; fresh vegetative bacterial endocarditis mitral, aortic, tricuspid valves; acute splenic tumor; glomerular nephritis; meningitis.

TABLE I

DATE	AUTHORS	NO. CASES SEX AGE	CLINICAL COURSE	ANTE-MORTEM BLOOD CULTURES
1928	Rost and Fisher[33]	(1) M. 8	Subacute, 9 weeks (chronic cardiac disease) Fever, emboli, mitral lesion	*H. influenzae* (*H. para-influenzae* not excluded)
1929	Cabot[34]	(1) M. 55	Acute, 32 days	*H. influenzae* (*H. para-influenzae* not excluded)
1931	Frank[35]	(1) M. 32	Subacute, 2 months Mitral stenosis and insufficiency; fever, petechiae, splenic tumor, embolic nephritis	*H. influenzae* 5 times from blood. (*H. para-influenzae* not excluded)
1931	Loewenberg and Goldburgh[36]	(1) F. 24	Subacute, 8 weeks	*H. influenzae* (*H. para-influenzae* not excluded in one out of six cultures)
1932	Fothergill, Sweet and Hubbard[20]	(2) M. 11	Subacute, 26 days Clinical evidence of cerebral abscess	Hemolytic, hemophilic bacillus ("Bacillus X"—Pritchett & Stillman, 1919) *H. influenzae*, hemolytic
		F. 10	Chorea and articular rheumatism, heart murmur 3 years before; fever, leucocytosis, enlarged spleen, hematuria, petechiae, 44 days	Hemolytic hemophilic bacillus on 2 occasions. *H. influenzae*, hemolytic
1932	Fiessinger and Arnaudet[37]	(2) F. 32	Articular rheumatism age 19. Fever, subcutaneous nodules, anemia, embolic phenomena, enlarged spleen. Mitral systolic and diastolic murmurs; 33 months.	*H. influenzae* (*H. para-influenzae* not excluded) from blood 14 months before death, and again 7 months before death
		M. 32	Fever, anemia, cardiac enlargement, aortic diastolic murmur. (Articular rheumatism, age 21.) Hematuria, edema 5 months	*H. influenzae* (*H. para-influenzae* not excluded) on one occasion
1933	Fiessinger and Albeaux-Fernet[38]	(2) M. 34	Several attacks articular rheumatism in youth. Fever, anemia, anasarca, increasing mitral systolic murmur. 5 weeks	*H. influenzae* (*H. para-influenzae* not excluded) on one occasion
		M. 44	Subacute, 3 months	None
1933	De Santo and White[19]	(1) F. 32	Acute, 5 weeks	Hemolytic hemophilic bacillus ("Bacillus X"—Pritchett and Stillman, 1919) positive in 2 out of 3 cultures. *H. influenzae*, hemolytic

—CONT'D

POST-MORTEM BLOOD CULTURES	AUTOPSY FINDINGS
None	No autopsy.
Same as ante-mortem from vegetations	Acute bacterial endocarditis; acute myocarditis; septic infarcts of kidneys and spleen; focal glomerulonephritis.
None	No autopsy.
Same organism from vegetations and from heart's blood	Vegetative bacterial endocarditis of mitral and aortic valves; moderate cardiac dilatation and hypertrophy; embolic pneumonia; acute splenic tumor; infarcts of kidneys and ? glomerulonephritis.
No culture. Morphology: Gram-negative bacilli	Heart only: vegetative bacterial endocarditis of mitral and aortic valves; acute and chronic focal myocarditis.
None	No autopsy.
None	No autopsy
None	No autopsy
None	No autopsy
No culture. Morphology: Small, Gram-negative rods in vegetations	Vegetative bacterial endocarditis aortic valve.
No cultures. Morphology: Small, Gram-negative rods in vegetations and in emboli in kidneys	Vegetative endocarditis of mitral valve; focal embolic myocarditis; pericardial effusion; infarcts of kidney and spleen.

TABLE I

DATE	AUTHORS	NO. CASES SEX AGE	CLINICAL COURSE	ANTE-MORTEM BLOOD CULTURES
1935	Stuart-Harris and others[22]	(4) F. 28	Subacute, 7 months	*H. para-influenzae* on 4 occasions
		F. 30	Subacute, 5 months Fever, anemia, embolic phenomena kidneys, brain	*H. para-influenzae* on 4 occasions
		M. 44	Subacute, 12 months	*H. para-influenzae* on 4 occasions
		F. 27	Subacute, 9 weeks	*H. para-influenzae* on 2 occasions
1935	Fox[24]	(1) F. 40	Subacute, 5 weeks	Hemolytic hemophilic bacillus ("Bacillus X"—Pritchett and Stillman, 1919). *H. para-influenzae*, hemolytic
1936	Lemierre[39]	(1) F. 22	Subacute, 3 months Fever, general malaise, signs of valvular damage. Embolic phenomena	*H. influenzae*. (*H. para-influenzae* not excluded)
1937	Lichty[23]	(1) M. 14	Subacute, 11 weeks	Hemolytic hemophilic bacillus ("Bacillus X"—Pritchett and Stillman, 1919) on 6 occasions out of 8. (*H. para-influenzae*, hemolytic)
1938	Miles and Gray[25]	(2) F. 28	Subacute course 15 (?) days	*H. para-influenzae*, nonhemolytic, on 3 occasions
		F. 41	Subacute course 34 (?) days	*H. para-influenzae*, nonhemolytic, on 3 occasions
1939	Authors' Cases	(2) M. 40	Chronic course; low-grade fever, mitral murmur, anemia, embolic phenomena, chronic meningitis, 330 days	*H. para-influenzae*, nonhemolytic, on 2 occasions
		F. 15	Recurring attacks pneumonia, chills and fever, anemia, systolic and diastolic pulmonic murmurs, 120 days	*H. para-influenzae*, nonhemolytic, on 9 occasions

—CONT'D

POST-MORTEM BLOOD CULTURES	AUTOPSY FINDINGS
Pneumococci only (cultures not made until 2 days after death). Smears from vegetations showed masses of Gram-negative rods	Vegetative endocarditis of aortic valve. Lobar pneumonia. Purulent meningitis.
None	No autopsy
H. para-influenzae from heart's blood. Masses of Gram-negative rods in smears of vegetations	Vegetative bacterial endocarditis of endocardium of left ventricle and aortic valve; splenic infarcts.
H. para-influenzae from heart's blood, and from spleen and kidney infarcts	Vegetative endocarditis. Infarcts of spleen and kidneys.
Cultures of heart's blood, lungs, spleen negative. Smears from endocardial vegetations showed small, Gram-negative bacilli	Vegetative (bacterial) endocarditis of mitral and aortic valves; cardiac hypertrophy; acute splenic tumor and infarcts of spleen; lobular pneumonia; acute glomerular nephritis; thromboses of right renal and right internal carotid arteries.
None	No autopsy
No cultures. Smears and sections of heart valves showed small, Gram-negative bacilli	Vegetative (bacterial) endocarditis of mitral and aortic valves, multiple infected emboli of heart, liver, spleen, kidneys, and left common iliac artery; cardiac hypertrophy and dilatation, mural thrombi in right auricle; pulmonary emboli; subacute glomerulonephritis and infected renal infarcts; lobular pneumonia.
None	Vegetative and ulcerative mitral endocarditis; lobular pneumonia; focal embolic nephritis.
None	Old (? rheumatic) mitral stenosis; vegetative (bacterial) endocarditis of mitral valve; bronchiectasis and atelectasis lower lobe left lung; infected infarcts spleen, brain, kidneys.
H. para-influenzae, nonhemolytic, from heart's blood, endocardial vegetations, and spleen	Vegetative (bacterial) endocarditis of mitral valve and auricular wall; acute and chronic meningitis; acute glomerular nephritis, infected infarcts of spleen and kidneys; acute splenic tumor.
H. para-influenzae, nonhemolytic, from heart's blood, endocardial vegetations, spleen and lungs	Vegetative (bacterial) endocarditis of pulmonic valve; multiple focal necroses of lungs; acute glomerulonephritis; acute splenic tumor; focal petechial cerebral hemorrhages.

Pfeiffer[1] was unable to cultivate the organism except in the presence of blood pigment, but Grassberger,[6] in 1898, reported cultivation of the organism in symbiosis with *Staphylococcus aureus* in media containing hematin. Olsen,[7] in 1920, showed that growth of *H. influenzae* occurred only in media giving a positive peroxidase reaction. In 1920, Fildes[8] grew the organism in media enriched by a peptic digest of blood, and, in 1921, he[9] demonstrated that two factors were essential for the growth of the organism. One factor was present in the clear supernatant fluid, and the other in the brown hematin deposit. These two factors were designated X and V by Thjötta and Avery,[10] in 1921. The V factor is relatively heat-labile, and is found in blood, in cultures of many bacteria, and in yeast and vegetable cells. The X substance is heat-stable, gives a positive peroxidase test, and is found in blood and raw potatoes. Rivers and Poole,[11] independently, in 1921, showed that two accessory factors are necessary for the growth of influenza bacilli; that one is present in filter-sterilized yeast extract, and the other in autoclaved extract of blood. Rivers,[12] in 1922, found that Friedberger's *B. hemoglobinophilus canis* required the X factor, and that two strains of *B. influenzae* isolated from patients required only the V factor. He designated the strains requiring only the V factor as *H. para-influenzae*. Later, in 1923, Rivers and Bayne-Jones[13] isolated from the throats of healthy cats six strains of influenza bacilli that required only the V factor for growth. Pritchett and Stillman,[14] in 1919, described a Gram-negative, aerobic, nonmotile, hemophilic bacillus and called it bacillus X. Rivers and Leuschner,[15] in 1921, tested a similar organism and found that it required both X and V growth accessory factors. Fildes,[16] however, in 1924, tested fourteen strains of hemolytic influenza bacilli and found that thirteen out of fourteen required only the V factor; the remaining strain required X and V. The thirteen strains requiring only the V factor grew on ordinary media in symbiosis with staphylococci, and also with *B. hemoglobinophilus canis* on media containing the X factor. Fildes believed that this fact indicated that *B. hemoglobinophilus canis* synthesizes the V factor. In 1927, Valentine and Rivers[17] studied thirty-four strains of hemophilic bacilli isolated from twenty-six patients suffering from chicken pox, measles, influenza, and miscellaneous conditions. Nineteen of the strains were nonhemolytic, and fifteen were hemolytic. Seventeen of the nonhemolytic strains required both X and V growth accessory factors, and, hence, were similar in every respect to the organism usually accepted as the Pfeiffer bacillus. Two of the nonhemolytic strains were cultivated easily when V factor alone was present, and, hence, corresponded with Rivers' *H. para-influenzae*. Of the fifteen hemolytic strains, ten grew well in broth to which only V factor had been added, whereas three strains required both X and V factors for growth. The remaining two strains were not viable after three or four transplants in broth containing both yeast extract and hematin.

On the basis of the experiments quoted, Valentine and Rivers[17] proposed the following classification of hemophilic bacilli:

A. Requiring the addition of X and V to the media:
B. influenzae (Hemophilus influenzae).
1. Nonhemolytic.
2. Hemolytic.

B. Requiring the addition of V only:
B. Para-influenzae (Hemophilus para-influenzae).
1. Nonhemolytic.
2. Hemolytic.

C. Requiring the addition of only X to the media:
B. hemoglobinophilus canis (Hemophilus canis).

D. Requiring the addition of neither X nor V to the media:
B. pertussis (Hemophilus pertussis).

The organisms in the cases of Miller and Branch,[18] De Santo and White,[19] and Fothergill, and others,[20] required both X and V factors for growth, and, hence, would be classified as *H. influenzae* (hemolytic). The organisms in the cases of Russell and Fildes,[21] Stuart-Harris and others,[22] Lichty,[23] Fox,[24] Miles and Gray,[25] and in our own cases required only V factor, and, hence, would be classified as *H. para-influenzae.*

Since the original report of Miller and Branch,[18] in 1923, four cases of endocarditis caused by *H. influenzae* (hemolytic) have been reported. Since the original report of Russell and Fildes,[21] in 1928, there have been reports of nine cases, including our own, of endocarditis caused by *H. para-influenzae* (hemolytic and nonhemolytic).

Reference to Table II will show that the average duration of the illness in the case in which the organism was *H. para-influenzae* (nonhemolytic) was 146 days, in those in which it was *H. para-influenzae* (hemolytic), 56 days, and in those in which it was *H. influenzae* (hemolytic), 39 days. Because there have been no cases reported which fulfill the requirements for inclusion in the *H. influenzae* (nonhemolytic) classification, we are unable to estimate the average duration of such infections. However, if it is true that *H. influenzae* (nonhemolytic) (bacillus of Pfeiffer) was most pervalent during the known influenza epidemics, it seems reasonable to surmise that in the cases of Jehle[3] and of Malloch and Rhea[26] the disease was caused by this organism. The duration of the illness in these three cases was 28 days, 13 days, and 6 days, respectively, so that the endocarditis would be classed as acute.

CLINICAL FEATURES

The clinical features of the disease, which may be acute, subacute, or chronic, do not differ in any important aspects from those of other etiologic types of bacterial endocarditis. It is our impression, derived

TABLE II

DURATION OF INFECTION WITH *H. influenzae* AND *H. para-influenzae* EXPRESSED IN DAYS

AUTHORS	H. INFLUENZAE		H. PARA-INFLUENZAE	
	HEMOLYTIC	NON-HEMOLYTIC	HEMOLYTIC	NON-HEMOLYTIC
Miller and Branch	51			
Fothergill, et al.	26			
	44			
De Santo and White	35			
Russell and Fildes				28 (?)
Stuart-Harris, et al.				210
				150
				365
				63
Miles and Gray				15 (?)
				34 (?)
Authors' Cases				330
				120
Fox			35	
Lichty			77	
	average		average	average
	39		56	146

from the clinical and cultural evidence presented in the literature and our own experience, that *H. influenzae* (nonhemolytic or hemolytic) is the most virulent member of the group and tends to produce an acute and rapidly fatal endocarditis; that *H. para-influenzae* (nonhemolytic) is least virulent, tending to produce a subacute or chronic form of the disease characterized by acute symptoms only in the terminal stages of the illness; and that *H. para-influenzae* (hemolytic) is intermediate. It seems probable that the majority of the cases reported in the literature as instances of infection with *H. influenzae* were, in reality, instances of infection with *H. para-influenzae* (nonhemolytic). The symptomatology simulates that of other forms of bacterial endocarditis, in that intermittent chills and fever, sweats, loss of weight, and petechiae are common, and because specific local symptoms depend upon the organs involved in the process of embolism. The cardiac findings naturally depend upon the degree and extent of individual valvular involvement. Leucocytosis of moderate to marked degree is usual, and in striking contrast to uncomplicated epidemic influenza. The clinical diagnosis rests upon the history of chills and fever, the physical signs of a cardiac lesion, evidence of embolism, and the demonstration of the specific organism in the blood stream. The course is progressive and uniformly fatal; no instances of recovery have been reported. Treatment with anti-influenzal serum has not been shown to influence the infection. We are unaware of any cases in which the patient was treated with sulfanilamide or its derivatives, except the two cases of our own. In Case 1, there were definite, transient improvement and disappearance of the signs and symptoms of meningitis, but relapse occurred several days after the drug was discontinued. In Case 2, the exhibition of sodium disulfanilamide was followed by an afebrile period of nine days,

during which two blood cultures were sterile, and there was marked clinical improvement. Relapse occurred here also, and the patient died twelve days later.

PATHOLOGY

Post-mortem studies have revealed, in general, the lesions usually found in endocarditis caused by streptococci. The endocardial vegetations are often, but not always, superimposed on the valvular lesions of rheumatic endocarditis, and they are of the vegetative, ulcerative type. Embolic phenomena in the skin, lungs, kidneys, spleen, and brain are common. Acute glomerulonephritis is a frequent occurrence. Apparently, meningitis occurs more frequently than in cases of endocarditis caused by alpha streptococci. In the thirty-six cases reviewed in this report there was unmistakable clinical or necropsy evidence of meningitis in five cases (14 per cent). In several other cases there was suggestive clinical evidence of meningitis, but in these cases no necropsy was done. The high incidence of meningitis, often of marked chronicity, suggests that infection of the leptomeninges antedates, in some cases, the endocardial lesions.

CONCLUSION

Two cases of bacterial endocarditis caused by *H. para-influenzae* (nonhemolytic) are reported in detail. A brief review of the clinical, pathologic, and bacteriologic features of endocarditis caused by the influenza group of organisms is presented.

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THE ROENTGENKYMOGRAM IN MYOCARDIAL INFARCTION

I. The Abnormalities in Left Ventricular Contraction

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IT HAS been adequately established[1-4] that there are changes in cardiac pulsation in the presence of myocardial infarction which can be demonstrated by roentgenkymographic examination. The purpose of the present report is to establish the value of this method of examination from a study of a large series of cases, and to describe the sequence of the kymographic abnormalities as they are observed in serial records, and correlate them with the various stages of the disease.

MATERIAL

Two hundred cases of typical coronary artery occlusion were studied. The diagnosis was established by clinical and electrocardiographic observations. In eighty-five cases the lesion was classed as recent, i.e., the attack had occurred within two months of the time of examination. In the remaining one hundred fifteen cases the lesion was classed as old. All of the patients in both groups had been under observation at Mt. Sinai Hospital during their acute attacks.

TECHNIQUE

A standard, multiple-slit kymographic grid was employed. In most instances a grid was used in which the slits were 18 mm. apart; in a few cases a 12 mm. grid was employed. The slits were 0.4 mm. in width. The casette moved down behind the grid. The kymograms were made under the following technical conditions: 100 kilovolts, 100 milliamperes, 2 to 3 seconds exposure (with the 18 mm. grid), 4-foot tube-film distance, and high-speed intensifying screens. A single-phase generator of the 4-valve tube type was used with a shock-proof, water-cooled tube. In most cases both a posteroanterior and a left oblique kymogram (30°) were made.

NORMAL VARIATIONS

In the normal subject, systolic contraction of the left ventricle is recorded on the roentgenkymogram as a uniform medial movement of the left cardiac contour, occupying about 0.2 second. Aortic distention is used as a guide to the onset of ventricular systole (Fig. 1 *A* and *B*). Diastole of the ventricle is recorded as a lateral movement. The speed of the movement and the shape of the curve vary considerably in normal subjects. It has not been possible yet to classify all of the variations into definite groups.

Variations in the pulsations of the apex and base of the left ventricle are observed in normal individuals. In the posteroanterior view, most

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normal kymograms show a larger amplitude at the apex than at the base; in some, however, the amplitude is smaller at the apex. This does not necessarily mean that there is a volumetric difference in contraction between the apex and the base, for the roentgenkymogram merely represents the projected record of the pulsation in one plane, and the angle that the line of the motion makes with the surface of the grid varies at different segments of the heart. However, the diminution or exaggeration in pulsation which is seen as one proceeds toward the apex is uniform; there are no sudden or localized changes. The onset of systole at the base slightly precedes that at the apex.

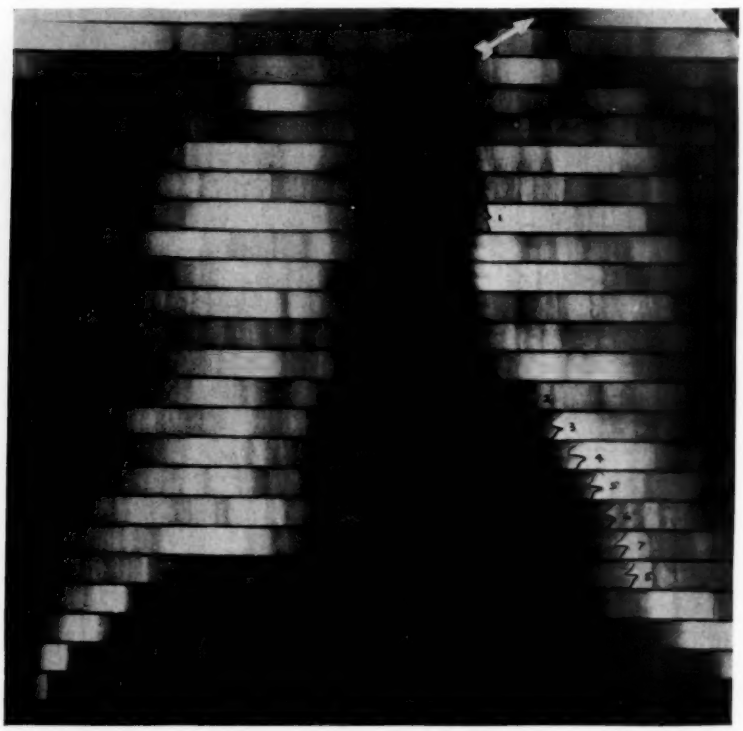

Fig. 1.—Normal roentgenkymogram, from a normal man, 50 years old.
A, Posteroanterior view.
B, Left oblique view.
In the upper right-hand corner a timing marker (arrow) is seen. The distance between each peak represents 0.2 sec.

A slow or a rapid systole is found in valvular disease or in functional disease of the heart (Fig. 2 *A* and *B*). A slight lateral movement immediately preceding systole is sometimes found normally, although perhaps more frequently in hypertension (Fig. 2 *D*). A short lateral movement at the end of systole is a normal occurrence which Hirsch[5] has shown corresponds most likely to the second heart sound (Fig. 2 *F*). A double movement in diastole may be normal, although it is sometimes seen in ventricular hypertrophy (Fig. 2 *I*). These smaller variations

which are superimposed upon the larger movements of systole and diastole must be differentiated from the abnormalities to be described below.

ABNORMALITIES IN MYOCARDIAL INFARCTION

In 75 per cent of the 200 cases of myocardial infarction the following abnormalities were found, and were considered characteristic:

(1) Diminution or absence of pulsation in a localized segment of the left ventricular contour (Fig. 3).

(2) Systolic expansion, either total or partial, over one or more segments of the lower left contour. Complete systolic expansion is indicated by lateral movement at the onset of systole, and the contour remains in the lateral position throughout systole (Figs. 2 *G* and 4). Partial systolic expansion is shown by

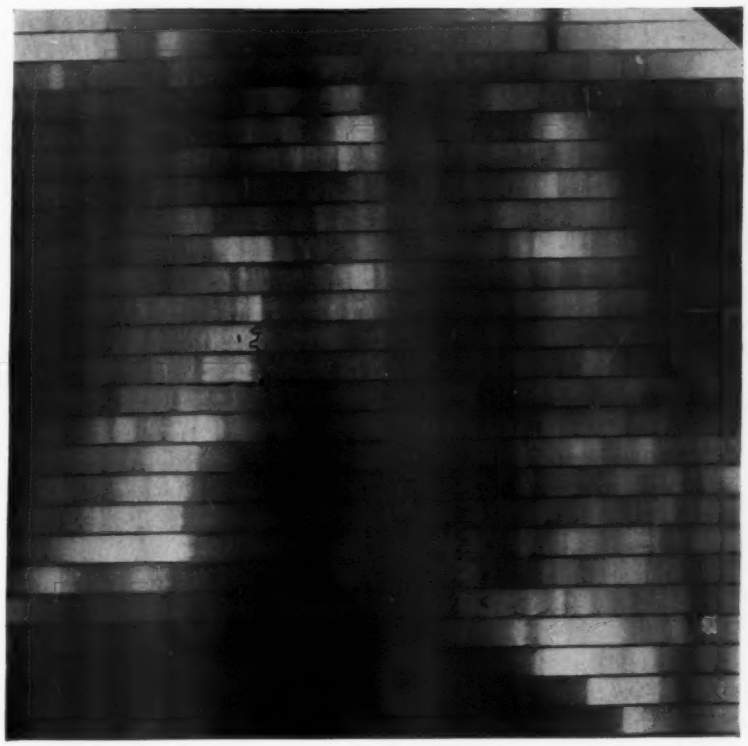

Fig. 1*B*.

lateral movement early in systole. This may appear as a delay or lag in the completion of systole, so that the curve of systole resembles a stepladder (Figs. 2 *C* and 5). In some cases systole begins at the usual time, but is followed immediately by lateral movement, producing what the French[3] have called an M-shape curve (Fig. 2 *L*).

(3) Diastolic splintering, as shown by marked irregularities in diastole (Fig. 2 *J*).

Equivocal changes included the following: generalized diminution in pulsation, slight localized diminution in pulsation, slight irregularities in diastole, and partial expansion not definitely in early systole. Table I gives the incidence of the findings.

TABLE I

ROENTGENKYMOGRAPHIC OBSERVATIONS IN 200 CASES OF MYOCARDIAL INFARCTION (P-A VIEW)

	RECENT INFARCTION	OLD INFARCTION	ALL CASES
Number of Cases	*85*	*115*	*200*
1. Systolic expansion	46 (54%)	51 (44%)	97 (48.5%)
2. Partial systolic expansion	9 (10.5%)	18 (15.5%)	27 (13.5%)
3. Absence or marked diminution	8 (9.5%)	17 (15%)	25 (12.5%)
4. Moderate diminution or irregularity	10 (11.5%)	15 (14%)	26 (13%)
5. Normal	12 (14%)	13 (11%)	25 (12.5%)
Total marked abnormalities (1, 2, 3)	63 (74%)	86 (75%)	149 (74.5%)

THE ROENTGENKYMOGRAM IN ACUTE INFARCTION

The early changes which occur in myocardial infarction were studied in thirty-two patients on whom roentgenkymograms were obtained during the first or second week following the onset of the attack of coronary occlusion. In addition, in most of these cases serial roentgenkymograms were obtained at weekly or biweekly intervals. It is seen in Table II that

TABLE II

ROENTGENKYMOGRAPHIC OBSERVATIONS DURING THE ACUTE STAGE OF MYOCARDIAL INFARCTION

(SERIAL STUDIES IN 32 CASES)

INITIAL CHANGES	SUBSEQUENT ABNORMALITIES
First and second week	Third to eighth week
10 Systolic Expansion	7 Systolic Expansion 3 Unknown
1 Partial Systolic Expansion	1 Complete Systolic Expansion
9 Marked Diminution	2 Complete Systolic Expansion 2 Partial Systolic Expansion 3 Marked Diminution 2 Unknown
3 Moderate Diminution	2 Complete Systolic Expansion 1 Unknown
2 Slight Diminution or Irregularity	1 Moderate Diminution 1 Normal
7 Normal	2 Systolic Expansion 1 Marked Diminution 2 Normal 2 Unknown

in ten of the thirty-two cases systolic expansion appeared as early as the first or second week. This persisted during the following three to eight weeks in all of the cases in which the roentgenkymogram was

repeated. In one case, partial systolic expansion which was observed during the first week progressed to complete systolic expansion during the third week. Moderate to marked diminution in pulsation was present during the early stages in twelve cases; in four of these it progressed to complete, and, in two, to partial, systolic expansion. In nine cases the initial roentgenkymogram was normal or showed equivocal changes; two of these patients subsequently developed complete paradoxical pulsation, and two developed moderate to marked diminution.

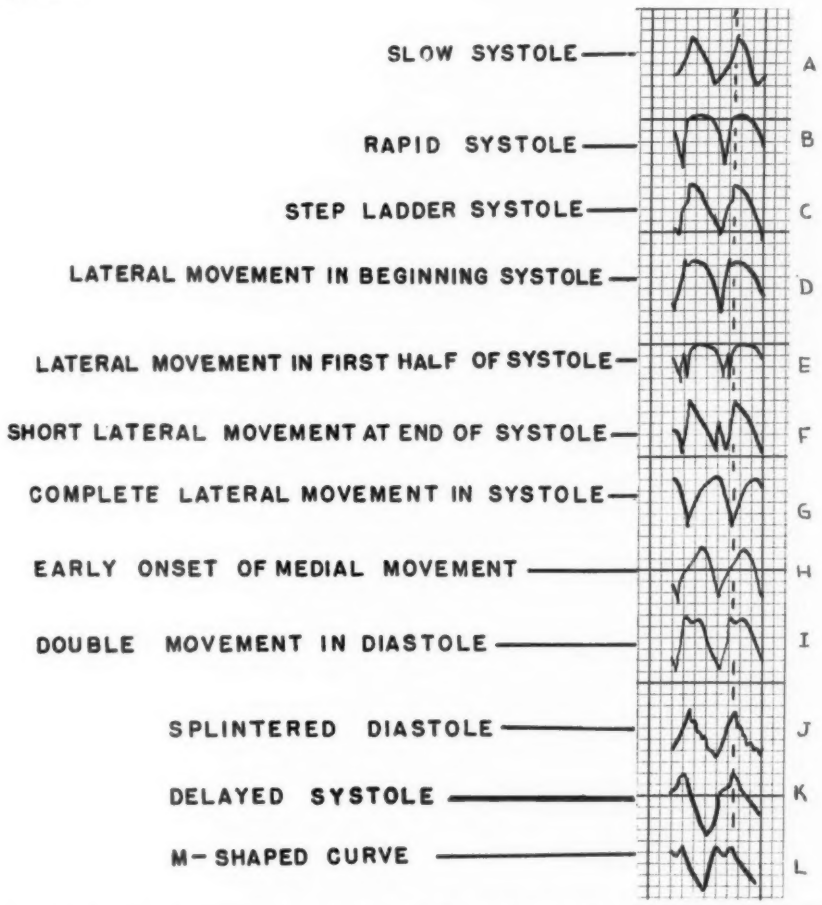

Fig. 2.—Normal and abnormal variations in the form of left ventricular pulsations.

Although the pulsations in the early stages are often normal or only slightly abnormal, in the majority of cases they become progressively impaired during the subacute stage, when complete or partial systolic expansion may be noted. In several cases a definite progression was observed in serial kymograms. Normal pulsations were found during the first week, moderately or markedly diminished pulsations in the second or third week, absence or partial reversal of pulsation in the

third or fourth week, and, finally, complete systolic expansion in the fourth or fifth week. In a few instances, serial roentgenkymograms showed that the cardiac contractions remained normal for as long as two or three months, when definite abnormalities finally became evident. This suggests that both softening of the ventricular wall by acute myomalacia, and replacement fibrosis, with thinning, may be associated with abnormal ventricular contraction. Definite myocardial infarction produces no kymographic changes in a minority of cases. Slight variations from the normal early in the attack may have considerable significance, but a single examination does not suffice to evaluate them.

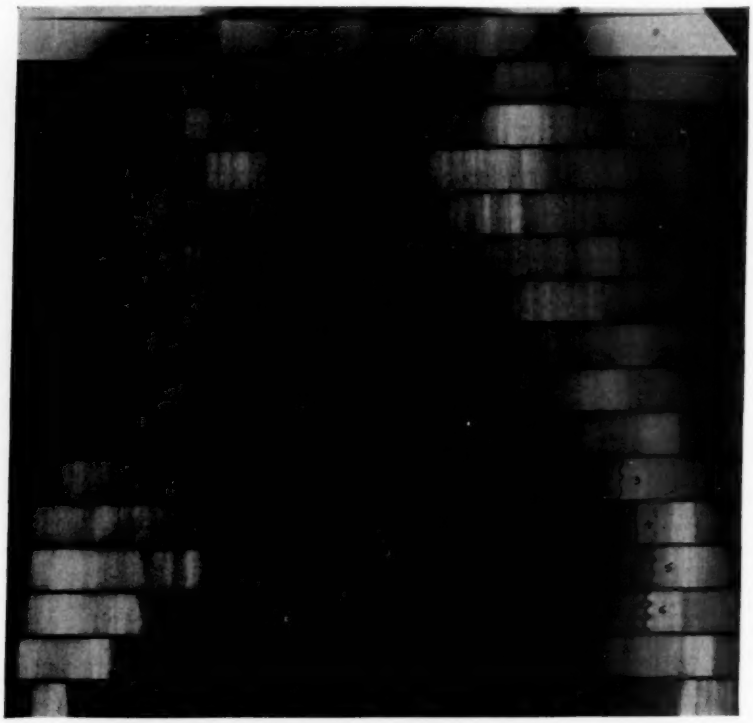

Fig. 3.—Posteroanterior roentgenkymogram from a man 53 years old. Coronary artery occlusion one week previously. Localized diminution in pulsation is seen in interval four of the left ventricular contour, and systolic expansion in intervals five and six.

THE ROENTGENKYMOGRAM IN OLD MYOCARDIAL INFARCTION

The evidence in Table I suggests that the incidence and type of kymographic abnormalities were the same in cases of recent and old myocardial infarction. The distribution of abnormalities at various stages following recovery was studied. In a large group of cases, serial records were obtained at intervals of one to four years after recovery from the attack of coronary occlusion. It is seen in Table III that the incidence of abnormalities at these various stages was approximately

the same as during the acute stage, and remained the same throughout the follow-up period. Of twenty-two patients who were examined four to twelve years after their attack of coronary occlusion, sixteen still showed evidence of previous infarction, in the form of complete or partial systolic expansion. It is probable that most abnormalities remain at least for many months or years following the coronary occlusion.

Abnormalities in pulsation which were present during the acute stage of the attack usually persisted, and in some instances they became more marked in the chronic stage. Thus, in a series of thirty-four patients who were examined serially during the acute attack and for one-half to two years after recovery (Table IV), partial systolic

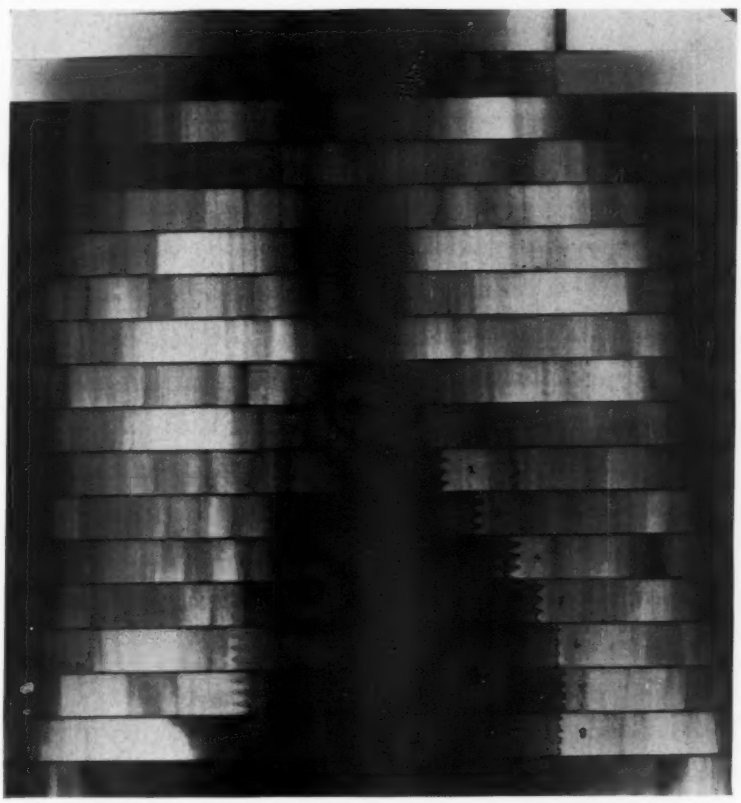

Fig. 4.—Posteroanterior roentgenkymogram from a man 37 years old. Coronary artery occlusion four months previously. Diminution in pulsation seen in interval six, and systolic expansion in intervals seven and eight.

expansion became complete after five months in one case; five patients with marked diminution of pulsation developed complete systolic expansion, and two patients with normal roentgenkymograms during the first two months developed complete or partial systolic expansion at the fourth and eighteenth months, respectively.

TABLE III

COMPARISON OF ROENTGENKYMOGRAMS OBTAINED DURING DIFFERENT STAGES OF MYOCARDIAL INFARCTION

STAGE OF INFARCTION	NUMBER OF RECORDS	COMPLETE OR PARTIAL SYSTOLIC EXPANSION	MARKED DIMINUTION OF PULSATION	TOTAL SIGNIFICANT ABNORMALITIES	NORMAL PULSATION
First week	21	38%	24%	62%	19%
Second to third week	30	67%	10%	77%	20%
Fourth to seventh week	65	54%	18%	72%	12%
Third to sixth month	49	55%	12%	67%	22%
Seventh to twelfth month	30	47%	17%	64%	17%
Second year	61	49%	20%	69%	20%
Third to fourth year	57	60%	12%	72%	18%
Fifth to twelfth year	22	73%	9%	82%	9%

TABLE IV

THE ROENTGENKYMOGRAM IN MYOCARDIAL INFARCTION FOLLOWING RECOVERY FROM THE ACUTE ATTACK

(SERIAL STUDIES IN 34 CASES)

Roentgenkymogram During Acute Stage (1 to 8 weeks)	*Roentgenkymogram after Recovery* (1½ to 2 years)
20 Systolic Expansion	11 Systolic Expansion
	6 Diminution with Irregularity
	3 Normal Pulsation
2 Partial Systolic Expansion	1 Complete Systolic Expansion
	1 Partial Systolic Expansion
5 Marked Diminution of Pulsation	2 Complete Systolic Expansion
	3 Marked Diminution
1 Moderate Diminution	1 Absence of Pulsation
2 Slight Diminution and Irregularity	2 Normal Pulsation
4 Normal Pulsation	1 Complete Systolic Expansion
	1 Partial Systolic Expansion
	2 Normal Pulsation

Not infrequently the abnormalities in pulsation were observed to disappear, or to become less marked. In the afore-mentioned series of thirty-four cases (Table IV), systolic expansion was observed in twenty cases during the acute or subacute stage of the attack, but it persisted in only eleven of these. Three follow-up roentgenkymograms became completely normal after recovery, and in six the systolic expansion regressed to diminution of pulsation with slight irregularities. It is suggested that healing of the myocardial infarct may be followed by complete or partial disappearance of the abnormalities in ventricular contraction; this probably occurs when healing is associated with very little residual fibrosis, which is a not uncommon postmortem finding.

COMMENT

The present study indicates that there is a definite place for cardiac roentgenkymography in the diagnosis and study of myocardial infarction secondary to coronary occlusion. In at least 75 per cent of the 200 cases, regardless of whether the infarct was recent or old, decided variations from the normal were found. The abnormalities often ap-

pear as early as the first or second week, and usually persist for many months or years following recovery. Therefore, the time of occurrence of the infarction could not be ascertained from the kymographic examination. Although the history and the electrocardiographic changes unquestionably remain the important diagnostic methods, the kymogram may be decisive in questionable cases. A detailed correlation of the roentgenkymogram, electrocardiogram, and clinical course is presented in another report.[6]

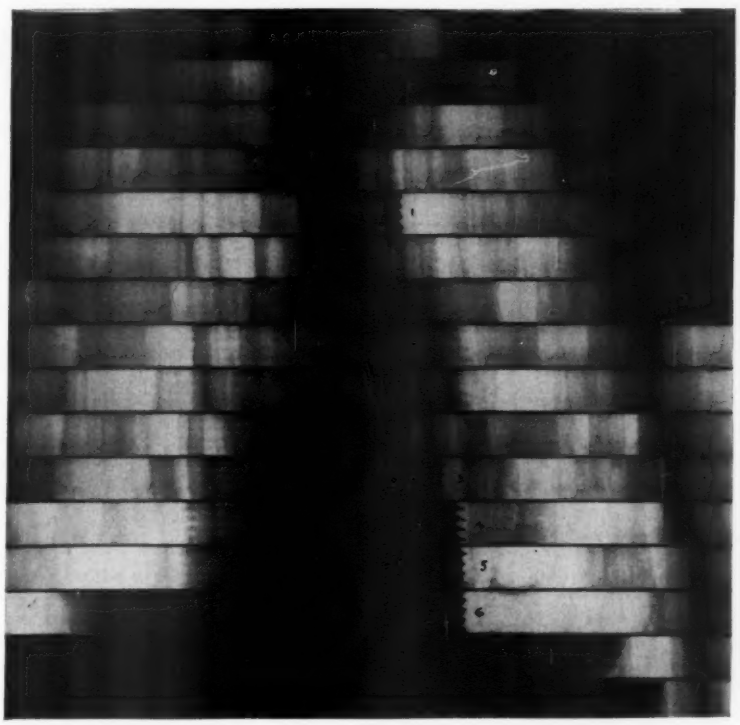

Fig. 5.—Left oblique roentgenkymogram from a man 52 years old. Coronary artery occlusion six weeks previously. Partial systolic expansion (stepladder effect) in interval four; lateral movement in midsystole in interval five.

The study has shown that considerable experience is necessary in the interpretation of the roentgenkymogram. In cases of subacute or old myocardial infarction, changes which are equivocal must be interpreted with great caution. In cases of recent infarction, however, slight variations from the normal should be regarded as significant until the course of the disease permits their correct evaluation. Partial or complete systolic expansion of a segment or of the entire left ventricular contour is most characteristic. Localized diminution or irregularity in pulsation, when it is not found at the apex alone, is very suggestive. Generalized diminution in pulsation and diminution which is localized to the apex, particularly when the heart is enlarged, cannot be regarded as characteristic, although in cases of recent occlusion this may prove to be significant.

There is no doubt that conditions other than myocardial infarction may produce the abnormalities which have been described above as characteristic. Technically, systolic expansion merely records the fact that this particular segment of the ventricle does not contract with the remainder of the ventricle. Our studies indicate that most often this occurs as a result of myocardial infarction, and hence that systolic expansion usually permits this diagnosis. However, ventricular aneurysm of rheumatic origin occurs occasionally. We have also observed two cases of what appeared clinically to be simple rheumatic aortic insufficiency, in which the roentgenkymogram revealed segmental paradoxical pulsation over the left ventricular contour. In syphilitic heart disease, rarely, similar changes have been noted,[7] presumably because of myocardial anoxemia secondary to narrowing of the coronary ostia. The paradoxical pulsation observed by Scott and Moore[8] in a case of pericardial tumor was caused by destruction of the underlying myocardium, so that it functioned as an aneurysm. A similar case has been noted by Gubner and Crawford.[9] Finally, myocardial fibrosis may possibly give rise to paradoxical movement, but, judging from our limited post-mortem material, this is uncommon; diminution in pulsation is more likely.

Systolic expansion does not necessarily indicate that there is an aneurysm of the left ventricle. The kymogram records the resultant movement of the segment. If, therefore, one segment of the heart does not move while the remainder of the ventricle is contracting, systolic expansion is recorded. Furthermore, as we have indicated in another publication,[6] there is reason to believe that we do not necessarily record the area of infarction when the contour shows systolic expansion; it is possible that the infarct is distant from the recorded segment.

SUMMARY

Characteristic abnormalities in left ventricular pulsation as recorded roentgenkymographically in 200 cases of myocardial infarction were as follows:

(1) Localized diminution or absence of pulsation.
(2) Complete systolic expansion or paradoxical pulsation.
(3) Partial systolic expansion, indicated by expansion early in systole or a delay in the completion of systole.
(4) Marked diastolic splintering.

These changes are found in cases of either recent or old infarction. In cases of recent infarction, even slight irregularities and diminution of pulsation may be of significance. These changes were found in 75 per cent of our cases of myocardial infarction, and are likely to be permanent, although progression and regression have been noted often. A persistently normal kymogram does not exclude the possibility of myocardial infarction. In most cases abnormalities appear

within three weeks of the attack, if they appear at all, but occasionally characteristic changes do not appear for several months. Characteristic roentgenkymographic findings usually permit one to make the diagnosis of myocardial infarction secondary to coronary artery occlusion.

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THE ROENTGENKYMOGRAM IN MYOCARDIAL INFARCTION

II. Clinical and Electrocardiographic Correlation

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IN A PREVIOUS report[1] we have shown that significant abnormalities are observed in the roentgenkymogram in three-fourths of all patients who have recent or old myocardial infarction as a result of coronary artery occlusion. In three-fifths of the cases the roentgenkymographic abnormality consisted of complete or partial reversal of ventricular pulsation, i.e., systolic expansion instead of contraction in the involved region of the left ventricle. In the remaining cases the abnormalities consisted of absence or marked diminution of ventricular contraction.

In this report we present a correlation of the roentgenkymographic observations, clinical course, and electrocardiographic changes observed in a series of 200 cases of coronary artery occlusion during the acute stage of the attack and during the stage of recovery. The series consisted of eighty-five cases of recent myocardial infarction in which the first roentgenkymogram was obtained from several days to two months after the attack, and 115 cases of healed infarction in which the first record was obtained from three months to four years after the occurrence of the infarction. Serial roentgenkymograms were taken in most of the cases, both during the acute stage and after recovery. All of the patients were under careful clinical observation in the hospital or in the special follow-up clinic devoted solely to patients who have sustained coronary artery occlusion. Numerous electrocardiograms, as well as observations of cardiac function, were made, usually simultaneously with the roentgenkymogram.

A. Correlation with the Severity of the Attack

The estimate of the severity of the acute attack of coronary occlusion was based upon the degree of shock and heart failure, as well as upon the symptoms. Correlation of these with the roentgenkymogram is presented in Table I. It is evident that characteristic changes, particularly complete systolic expansion, are most often present in the cases of severe myocardial infarction.

B. Correlation with the Degree of Recovery

The extent of recovery from an attack of coronary occlusion was gauged clinically by the residual disability, subsequent presence or absence of angina pectoris, tests for exercise tolerance, and vital capacity.

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TABLE I

CORRELATION OF ROENTGENKYMOGRAPHIC CHANGES AND SEVERITY OF THE ATTACK

SEVERITY OF ATTACK	MILD	MODERATE	SEVERE
No. of Cases	50	105	46
Characteristic Changes			
a. Complete systolic expansion	30%	48%	52%
b. Partial systolic expansion	20%	20%	20%
c. Marked diminution in pulsations	10%	13%	20%
Total	60%	81%	92%
Equivocal Changes	20%	8%	4%
Normal Kymogram	20%	11%	4%

TABLE II A

CORRELATION OF ROENTGENKYMOGRAPHIC CHANGES AND DEGREE OF RECOVERY

RECOVERY	GOOD OR COMPLETE	FAIR OR INCOMPLETE	POOR	ANOTHER ATTACK	CEASED
No. of cases	51	56	78	20	19
Characteristic Changes					
a. Complete systolic expansion	29%	36%	60%	60%	47%
b. Partial systolic expansion	22%	27%	15%	10%	16%
c. Marked diminution in pulsations	10%	14%	3%	25%	26%
Total	61%	77%	78%	95%	89%
Equivocal Changes	16%	11%	15%	5%	5%
Normal Kymogram	23%	12%	6%	5%	5%

TABLE II B

THE DEGREE OF RECOVERY CORRELATED WITH VARIOUS TYPES OF KYMOGRAPHIC ABNORMALITIES

KYMOGRAPHIC ABNORMALITIES	NO. CASES	DEGREE OF RECOVERY		
		GOOD	FAIR	POOR
Complete Systolic Expansion	82	18%	24%	57%
Partial Systolic Expansion	38	29%	39%	32%
Marked Diminution of Pulsation	15	33%	53%	13%
Total Marked Abnormalities	135	23%	32%	45%
None	24	46%	33%	21%

The evidence presented in Tables II A and B, in which these findings are correlated with the roentgenkymogram, shows that:

1. Characteristic roentgenkymographic changes are most often found in those who make a poor recovery (78 per cent), although it is noteworthy that the changes were present also in 61 per cent of the patients who made a good recovery.

2. There is a greater difference in the incidence of what may be considered a more advanced sign—that of complete systolic expansion. In only 29 per cent of those who made a good recovery was this sign present.

3. The kymogram was normal in only 6 per cent of those who made a poor recovery, but in 23 per cent of those who made a good recovery.

4. Significant abnormalities were present in all but two of the nineteen patients who died while under observation, and in all but two of the twenty patients who sustained a subsequent coronary occlusion. These cases are included also in the "poor recovery" group.

5. Good or complete recovery occurred twice as often in cases in which the kymogram was normal as in those in which there were significant kymographic abnormalities.

It is evident that, in individual cases, roentgenkymographic changes do not determine the prognosis. In general, however, characteristic changes are more likely to occur when recovery is poor than when it is good.

In thirty-four cases of the larger group, serial kymograms were made at frequent intervals during the acute stage and for several months or years following the attack. There were thirteen patients whose kymographic abnormalities disappeared or became less marked. Recovery was good in eight, and fair or poor in five. In twenty-one patients, or 62 per cent, the kymographic abnormalities were persistent or became more marked. In only two of these was recovery complete. These statistics suggest that persistence or progression of the abnormalities usually indicates that the recovery will be poor. However, a return to normal of the kymogram is often, but not necessarily, associated with good recovery.

C. CORRELATION WITH THE ELECTROCARDIOGRAM

In about 75 per cent of our cases of myocardial infarction, the roentgenkymogram showed definite abnormalities. Table III records the

TABLE III

ROENTGENKYMOGRAPHIC CHANGES IN CASES OF MYOCARDIAL INFARCTION IN WHICH THE ELECTROCARDIOGRAM WAS NORMAL

	EKG NORMAL DURING ACUTE STAGE OF ATTACK	EKG NORMAL FOLLOWING RECOVERY
No. of Cases	5	23
Roentgenkymogram:		
Complete systolic expansion	4	11
Partial systolic expansion	0	2
Marked diminution of pulsation	0	1
Moderate diminution of pulsation	0	4
Normal pulsation	1	5

roentgenkymographic observations in twenty-eight cases in which the electrocardiogram was normal during the acute attack or during recovery, but the signs and symptoms were typical of coronary artery occlusion. Of the five cases of Group A in which the electrocardiogram was normal during the acute stage of the attack, there was systolic expansion in four. In two of these, the electrocardiogram subsequently

developed the typical pattern of acute infarction; in two it remained normal. In Group B, the electrocardiogram was typical of acute infarction during the acute attack but returned to normal during recovery. In fourteen of the twenty-three cases, the abnormalities in pulsation persisted. In only five of the twenty-three cases was the kymogram entirely normal. In many other cases of our series the abnormalities in the electrocardiogram lost the distinctive pattern of myocardial infarction, but significant abnormalities in pulsations persisted.

In a previous section it was noted that in a group of thirteen patients whose kymographic abnormalities disappeared or became less marked, recovery was good in eight, and fair or poor in five. Typical electrocardiographic signs of myocardial infarction persisted in seven patients of this group despite the lessening of the kymographic changes.

D. CORRELATION WITH ELECTROCARDIOGRAPHIC LOCALIZATION OF THE INFARCTION

In ninety of the 200 cases, the electrocardiogram showed the Q_1T_1 pattern characteristic of anterior wall infarction, and, in thirty-two cases, the Q_3T_3 pattern indicative of posterior wall infarction. Signs of both anterior and posterior wall infarction were present in sixty-one cases. It seemed important to ascertain whether the location of the infarct, as determined electrocardiographically, bore any relation to the location of the abnormalities in the roentgenkymogram. In order to study the left ventricle as completely as possible by means of the roentgenkymogram, examinations were made in posteroanterior and left oblique positions. It is assumed that the left contour in the left oblique view represents a more posterior position of the left ventricle than in the posteroanterior view. The correlation of the kymogram in each view with the location of the infarct is given in Table IV, which reveals the following:

1. Characteristic changes were found in the posteroanterior kymogram as often in cases of posterior as in cases of anterior infarction. The incidence of the various types of abnormalities in each group is also approximately the same.

2. When the infarction was both anterior and posterior, the incidence of kymographic abnormalities was high (86 per cent), and paradoxical pulsation was present in 69 per cent. In only 3 per cent of this group were the kymograms entirely normal.

3. In cases of posterior infarction, the incidence of normal records in the posteroanterior view was only slightly higher than in anterior infarction.

4. Abnormalities were demonstrated in the left oblique view much less frequently than in the posteroanterior view, regardless of whether the site of infarction was anterior, posterior, or both. Complete systolic expansion was particularly less frequent; partial systolic expansion was relatively more common.

TABLE IV

CORRELATION OF ROENTGENKYMOGRAPHIC CHANGES AND SITE OF INFARCTION

EKG LOCALIZATION OF INFARCT	POSITION OF PATIENT*	NO. OF CASES	ROENTGENKYMOGRAPHIC CHANGES					
			COMPLETE SYSTOLIC EXPANSION	PARTIAL SYSTOLIC EXPANSION	ABSENCE OR MARKED DIMINUTION	TOTAL CHARACTERISTIC CHANGES	MODERATE DIMINUTION	NONE
Anterior	PA	90	39%	11%	20%	70%	15%	15%
	LO	64	19%	17%	2%	38%	14%	48%
Posterior	PA	43	39%	21%	7%	67%	12%	21%
	LO	34	14%	21%	9%	44%	12%	44%
Anterior and Posterior	PA	61	69%	10%	7%	86%	11%	3%
	LO	50	36%	18%	8%	62%	4%	34%
Unknown	PA	6						
	LO	5						

*PA—Posteroanterior position; LO—Left oblique position.

Further pertinent data concerning localization of the infarct were obtained by comparing the degree of abnormality in the two views in each case, as shown in Table V. It is seen that in 54 per cent of the

TABLE V

COMPARISON OF POSTEROANTERIOR AND LEFT OBLIQUE ROENTGENKYMOGRAM IN CASES IN WHICH THE SITE OF INFARCTION VARIED

LOCATION OF INFARCT	NO. OF CASES	PA VIEW SHOWS GREATER CHANGES			BOTH VIEWS POSITIVE	LO VIEW SHOWS GREATER CHANGES			BOTH VIEWS NEGATIVE
		PA+LO−	PA>LO	TOTAL		PA−LO+	LO>PA	TOTAL	
Anterior	64	38%	16%	57%	16%	1%	14%	15%	16%
Posterior	34	26%	26%	52%	18%	9%	3%	12%	18%
Anterior and posterior	50	30%	16%	46%	40%	0%	10%	10%	4%
Unknown	5								

cases of anterior infarction, and in 52 per cent of the cases of posterior infarction, the kymogram revealed abnormalities which were present in the posteroanterior view exclusively, or were more marked in this view. In 70 per cent of each group the posteroanterior kymogram showed characteristic changes. In only one case of anterior infarction and in three cases of posterior infarction were abnormalities visualized exclusively in the left oblique view. These data indicate that the roentgenkymogram is not a satisfactory method for localizing the site of the infarct. It is also evident that the posteroanterior view usually gives most of the data that can be obtained.

E. POST-MORTEM CORRELATION

In six cases in our series the hearts were examined at autopsy. The kymographic and pathologic observations in each case are presented in Table VI. The small number of post-mortem examinations makes it impossible to obtain accurate correlations. Multiple occlusions and infarcts were present in several cases, making the correlation more difficult. Nevertheless, several significant conclusions can be drawn from the data. All of the six patients who came to autopsy presented definite abnormalities in the kymogram. Complete systolic expansion in four cases could be correlated with large areas of infarction, or thinning, of the left ventricle. In these four cases the site of greatest infarction or thinning coincided with the site of the most marked abnormalities in pulsation. Of the two remaining cases in which only diminution or irregularities of pulsation were present in the kymogram, in one the infarct was small and situated posteriorly, and in the other there was diffuse fibrosis, more marked on the posterior wall. The kymographic abnormalities in these two cases were present only in the posteroanterior view.

A comparison of the accuracy of the electrocardiogram and roentgenkymogram in localizing the area of infarction can be made in Cases 2, 3, and 4. In Case 2 the electrocardiogram presented the Q_1 T_1 pattern

TABLE VI

CORRELATION OF ROENTGENKYMOGRAPHIC AND AUTOPSY OBSERVATIONS

CASE	SEX AND AGE	NO. OF ATTACK	TIME OF ATTACK BEFORE DEATH	EKG LOCALIZATION	ROENTGENKYMOGRAM	AUTOPSY OBSERVATIONS
1	M-54	1	2 years	Anterior		Acute and old infarction and aneurysmal dilatation of ant. wall and apex L.V. Recent infarction post. wall L.V. Recent and old occlusion of LAD and rt. cor. art.
		2	1 week	Ant. post.	PA—systolic expansion LO—not obtained	
2	M-44	1	6 years	Anterior		Acute and old infarction and aneurysmal dilatation of anterior wall L.V. and septum. Old infarction post. wall L.V. Acute and old occlusion LAD, old occlusion L. circumflex artery.
		2	3 years	Anterior	PA—systolic expansion over entire L.V. contour LO—slight irregularities	
		3	1 day	?		
3	M-63	1	2 years	Posterior		Old infarction apex and posterior wall L.V. Acute infarction anterior wall L.V. Acute and old occlusion LAD, old occlusion right coronary artery.
		2	1 year	Anterior	PA—marked diminution of pulsation LO—systolic expansion	
		3	1 week	Anterior?		
4	M-42	1	6 months	Anterior	PA—systolic expansion LO—systolic expansion	Old infarction and aneurysmal dilatation of anterior and posterior walls L.V. Organizing infarction posterior wall. Old occlusion LAD and right cor. artery.
		2	1 month	Posterior		
5	M-65	1	8 months	Posterior	PA—marked irregularity (partial systolic expansion) LO—normal	Old infarction posterior wall. Acute and old occlusion of right coronary artery.
		2	3 days	Posterior		
6	M-64	1	1 year	Ant. post.		Diffuse fibrosis left ventricle, especially posterior wall. Old occlusion LAD and right coronary artery.
		2	5 months	Ant. post.	PA—marked diminution with irregularities LO—normal	
		3	1 week	Posterior?		
7	F-60		3 months? Cardiac failure	Anterior?	PA—normal LO—not obtained	Scattered myofibrosis. Severe coronary sclerosis.
8	M-46		Cardiac failure? Severe hypertension	Anterior?	PA—moderate to marked diminution of pulsation LO—not obtained	Large heart. Scattered myofibrosis. Moderate coronary sclerosis.

of anterior wall infarction, and the kymogram revealed characteristic changes only in the posteroanterior view, but autopsy revealed an old posterior infarct, in addition to a large anterior infarct. In this case both methods failed to reveal the posterior infarct. In Case 3 the electrocardiogram presented signs of both anterior and posterior wall infarction, and the kymogram revealed abnormalities which were more marked in the left oblique view. These observations were corroborated by the autopsy, which revealed infarction of both surfaces of the left ventricle which was more extensive on the posterior wall. In this case both methods accurately localized the lesion. Finally, the electrocardiogram in Case 4 indicated an anterior infarct, but the kymogram showed marked abnormalities in the left oblique, as well as in the posteroanterior view, suggesting posterior infarction, also. The autopsy revealed not only infarction of the anterior wall, but also of the posterior wall of the left ventricle. It is clear from this correlation that both the electrocardiogram and the roentgenkymogram may fail to reveal the presence of multiple infarcts. It is also seen, however, that the kymogram may suggest infarction of both surfaces of the heart when the electrocardiogram is characteristic of infarction of only one surface.

Two other cases, not included in this series, have also been presented in Table VI. In both cases it was suspected clinically that coronary artery occlusion had occurred, but this was not corroborated at autopsy. In the first case (Case 7), the heart showed severe coronary sclerosis and scattered myofibrosis, but no coronary occlusion or infarction. The posteroanterior roentgenkymogram was normal. In the second case (Case 8), the heart was large as a result of long-standing hypertension. There was also moderate coronary sclerosis, with scattered myofibrosis. The posteroanterior kymogram revealed moderate to marked generalized diminution in pulsation over the left ventricular contour, but no systolic expansion. Hence marked cardiac enlargement without infarction may be associated with generalized diminution of pulsation in the kymogram.

COMMENT

Since the roentgenkymogram presents significant abnormalities in the great majority of cases of myocardial infarction, it should be of considerable diagnostic value. In a patient with a history suggesting coronary artery occlusion, recently or in the past, the discovery of abnormal ventricular pulsations in the kymogram should confirm the diagnosis despite the absence of typical electrocardiographic changes. Thus, in several patients with atypical attacks simulating noncardiac disease, and in several cases in which it was difficult to differentiate between acute coronary occlusion and angina pectoris, the roentgenkymogram pointed to the presence of myocardial infarction.

This was also true of patients who recovered from their attacks, and whose electrocardiograms, although remaining abnormal, were atypical and showed few or none of the characteristic features of infarction. A characteristic, abnormal roentgenkymogram, although not pathognomonic, may be considered diagnostic of infarction.

It was found that the kymogram not infrequently shows complete or partial regression of abnormalities in pulsation, even when the electrocardiographic abnormalities persist. Whether the kymogram in such cases affords a more delicate index of healing of the infarct than the electrocardiogram is not clear. On the other hand, we have seen that the electrocardiogram may return to normal while the roentgenkymogram shows persistent abnormalities. The former records changes in impulse conduction through the ventricular muscle, whereas the latter records changes in ventricular contraction. It is probable that healing of an infarct may be associated with recovery of contractility and not of conductivity, and vice versa.

Not only has the roentgenkymogram proved of diagnostic value in coronary occlusion, but also of prognostic significance. On a statistical basis, we have shown that if a patient has a normal roentgenkymogram during the acute stage of infarction, the clinical course is more likely to be mild, the recovery is more likely to be good or complete, and a recurrence of the coronary occlusion in the near future is less likely than if the patient has characteristic abnormalities of ventricular contraction. A good or complete clinical recovery is also more likely when the kymographic abnormalities disappear or become less marked.

It may be assumed that in cases of complete recovery from coronary artery occlusion the myocardial infarct or scar was of small extent. The fact that the roentgenkymogram was normal or showed only equivocal changes in a large number of patients who recovered completely, or almost completely, suggests that the kymogram is likely to remain normal if the infarct is small. Marked kymographic abnormalities, affecting a greater part of the left ventricular contour, are probably caused by a large infarct or extensive thinning of the ventricle. An acute myocardial infarct sufficiently extensive to produce congestive heart failure or severe shock usually produces marked abnormalities in ventricular pulsation in the roentgenkymogram.

A striking observation was that regardless of whether the infarct involved the posterior surface or the anterior surface of the left ventricle, as determined from the electrocardiographic pattern, the roentgenkymographic abnormalities were usually seen distinctly in the posteroanterior view. The location and type of abnormality in pulsation were similar regardless of the location of the infarct. In determining the effect on the roentgenkymogram, the extent of the infarct seemed to be of greater significance than the location. When multiple infarcts, or an extensive one involving both surfaces of the

left ventricle, were present, the ventricular pulsations recorded in the kymogram were usually abnormal.

Although an accurate correlation of the site of infarction and the location of the kymographic abnormalities could not be made from our studies, we believe that some clue to the site of infarction may be derived from a comparison of the changes in the posteroanterior and left oblique kymograms. Thus, it is our impression that when the abnormalities are present only in the posteroanterior view, the infarct is more likely to be anterior, although, in many cases, the electrocardiogram will indicate posterior infarction. When the abnormalities are visible only in the left oblique view, a posterior infarct should be suspected. When both views show changes, infarction of both surfaces is most likely. For diagnostic purposes, however, it should be sufficient to take only a posteroanterior kymogram, for, with only a few exceptions, if there is any abnormality in pulsation, it will be visualized in this view.

The frequent association of posterior infarction with abnormal pulsations in the posteroanterior kymogram raises the question whether these abnormal pulsations correspond to the site of the infarct. When the kymogram reveals systolic expansion in the supra-apical region, does this actually mean that there is an infarct in this region? Surely, an infarct or scar localized to the posterior, basal surface of the heart does not present anteriorly on the left ventricular contour. However, without post-mortem confirmation, the absence of an anterior infarct is not certain, even when the electrocardiogram is typical of posterior infarction, for multiple or unsuspected infarcts are common. In the absence of this possibility, the abnormal movements in the posteroanterior kymogram when there is a posterior infarct must be regarded, not as actual movements of the infarcted area, but as some form of transmitted pulsation from the posterior to the anterior or lateral surface of the left ventricle. A possible explanation rests in the anatomic structure of the heart. The superficial muscle layers are attached to the auriculoventricular ring posteriorly, and wind around the left ventricular margin and apex to the anterior surface, where they are inserted in the papillary muscles. It is possible to speculate that infarction or scarring posteriorly will deprive the spirally arranged muscles of their posterior fulcrum, and therefore the portion of the muscle in the apical region or along the left ventricular contour gives way with each systole of the heart, and passively expands or remains stationary instead of contracting.

SUMMARY

1. A correlation is presented of the roentgenkymographic observations, electrocardiographic changes, and clinical course in 200 cases of acute and old myocardial infarction secondary to coronary artery occlusion.

2. A close correlation was found between the incidence and degree of kymographic abnormalities and the clinical course, as judged by the severity of the attack and degree of recovery. The kymogram is usually normal when the attack is mild and the recovery good. Regression or complete disappearance of kymographic abnormalities is a good prognostic sign. The kymographic abnormalities are usually marked when the attack is severe and the recovery incomplete.

3. The roentgenkymogram not infrequently presents abnormalities characteristic of myocardial infarction when the electrocardiogram is normal or atypical. On the other hand, the roentgenkymogram may remain normal or return to normal, while typical electrocardiographic abnormalities persist. These two methods of examination therefore supplement each other.

4. The roentgenkymogram should prove to be of most diagnostic value during the acute stage, when the clinical course and electrocardiogram are not typical of coronary artery occlusion, and following recovery, when the characteristic signs of previous infarction have disappeared.

5. Posterior infarction produced abnormalities in the posteroanterior kymogram as often as did anterior infarction. In only a minority of cases of either anterior or posterior infarction were abnormalities visualized better in the left oblique kymogram than in the posteroanterior kymogram. A possible reason for this is discussed. When multiple infarcts were present, or one involving both surfaces of the left ventricle, the frequency and degree of kymographic abnormalities increased.

6. At post-mortem examination, systolic expansion in four cases could be correlated with a large area of infarction or thinning of the left ventricle. Diminution of pulsation occurred in one case in which there was a small posterior infarct, and in another in which there was diffuse myofibrosis.

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SEASONAL INCIDENCE OF CORONARY OCCLUSION IN A MILD CLIMATE

A Study Based Upon Autopsy Material

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THE seasonal variation in the frequency of attacks of coronary occlusion has been discussed in the medical literature during the past few years. Bean and Mills[1] have recently reported a group of cases and have reviewed the literature dealing with the seasonal occurrence of acute coronary occlusion. In Southern California the seasonal variation in temperature is much less than in the northeastern portion of the United States, where all of the reported studies were made. The present investigation was undertaken for the purpose of comparing the seasonal incidence of acute coronary occlusion in a mild, subtropical climate with the reported seasonal incidence in the north temperate regions of the United States.

MATERIAL

Between Jan. 1, 1929, and Feb. 28, 1939, there were 456,202 admissions to the Los Angeles County Hospital. During this same period, 41,260 patients died, and 16,395 autopsies were performed at the hospital. Because the date of coronary occlusion can be ascertained more accurately when a recent, unhealed infarct is found at the time of autopsy, only those patients with this type of myocardial infarct are included in this study.

The clinical and autopsy records of 501 patients made it possible to ascertain the date of onset of coronary occlusion with sufficient accuracy to tabulate the attacks according to calendar months. The review of autopsy records was extended two months in order to include patients whose infarcts occurred in the last month of the ten-year period from January, 1929, through December, 1938. In 485 of these 501 patients, coronary occlusion occurred in this ten-year period. The data relating to the time of the year when the attacks occurred are included in Table I and Fig. 1.

Most of the patients admitted to the Los Angeles County Hospital are indigent residents of Los Angeles County, so that seasonal migration of population has no significant effect upon our autopsy records. Since the consent for an autopsy is, as a rule, obtained by members of the clerical staff, and since the ratio of autopsies obtained to deaths which occur does not vary significantly with the seasons, this study of autopsy case records provides a fairly accurate sampling of the hospital deaths.

COMMENT

In reviewing the medical literature bearing on the seasonal incidence of coronary occlusion, Bean and Mills[1] found reports from Philadelphia, Pittsburgh, New York, and Boston, and added a series of cases of their

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own, collected in Cincinnati. The data as to the month of onset of 1,640 attacks of coronary occlusion in these five cities are included in Table I for comparison with the present series. The difference between the average mean temperatures of the coldest and hottest months of the year in Los Angeles from 1929 through 1938 was 16.4° F., whereas, in the report mentioned above, this difference for the northeastern cities was given as approximately 47° F. Despite the smaller temperature variation in Los Angeles, the incidence of acute coronary occlusion had practically the same seasonal variation as reported for the eastern cities.

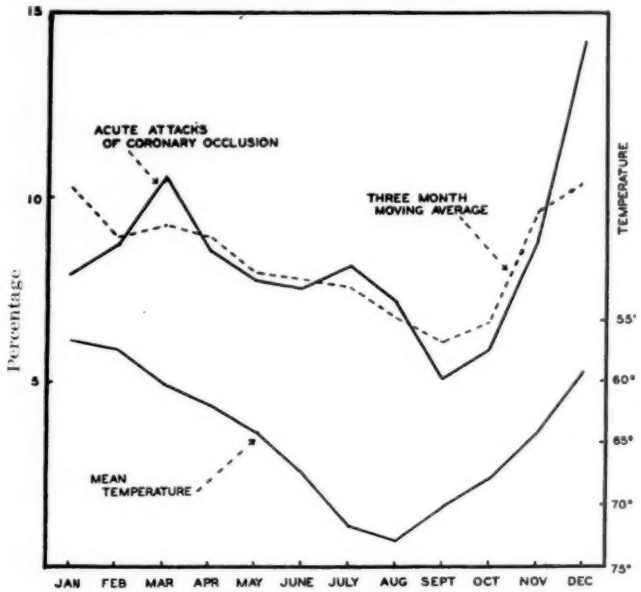

Fig. 1.—Percentage of coronary occlusions by months, compared with monthly mean temperature.

In both the reported series and the present series, the lowest incidence of coronary occlusion occurred in the month following the hottest month. The hottest month of the year was July in the eastern cities, and August in Los Angeles. Possibly very hot weather increases the likelihood of acute coronary occlusion. This possibility is apparently supported by the increase in the number of occlusions during July in both the reported and the present series; however, statistical analysis of the number of occlusions in the present series showed that the increase in July over June and August was not significant.

It was thought that, in the present series, the high average incidence of coronary occlusion during the month of December might have been accounted for by the holidays during and just preceding this month, but, judging from the weekly incidence, there was no significant correlation.

TABLE I

ACUTE CORONARY OCCLUSION

MONTH	PRESENT SERIES			REPORTED SERIES SUMMARIZED BY BEAN AND MILLS[1]	
	ACTUAL NUMBER OF OCCLUSIONS	NUMBER ON 31-DAY MONTH BASIS	PERCENTAGE OF TOTAL OCCLUSIONS	NUMBER ON 31-DAY MONTH BASIS	PERCENTAGE OF TOTAL OCCLUSIONS
January	39	39	7.9	183	11.2
February	39	43	8.7	151	9.2
March	52	52	10.6	138	8.4
April	41	42	8.5	134	8.2
May	38	38	7.7	137	8.4
June	36	37	7.5	100	6.1
July	40	40	8.1	115	7.0
August	35	35	7.1	93	5.7
September	24	25	5.1	137	8.4
October	29	29	5.9	133	8.1
November	42	43	8.7	153	9.3
December	70	70	14.2	166	10.0
Total	485			1,640	

Incidentally, there was no significant difference between the seasonal variation in the incidence of first occlusions and of fresh occlusions in patients who already had myocardial scars. There is apparently less seasonal variation in the frequency of acute coronary occlusion in patients over 70 years of age than in those under 70.

CONCLUSIONS

In the subtropical climate of Los Angeles, acute attacks of coronary occlusion are definitely more frequent in winter and early spring than in late summer and early fall.

Comparison with a series reported from a north temperate region seems to indicate that there are factors other than the degree of seasonal temperature variation. The most potent of these factors is probably the greater frequency of infections during the colder months.

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Department of Clinical Reports

TRICHINOSIS OF THE MYOCARDIUM

Report of a Case, With Autopsy Findings

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TRICHINOSIS of the myocardium has been a recognized entity since the discovery of larvae in heart muscle by Zenker[1] in 1860. Although various components of the cardiovascular system may be affected during the migration of the parasites, involvement of the heart is probably the most frequent and the most serious. Routine electrocardiograms in cases of clinically evident trichinosis indicate that some degree of involvement of the myocardium is more frequent than was formerly thought. Beecher and Amidon[2] found an incidence of 4.2 per cent in a series of forty-four cases of mild trichinosis. Spink,[3] however, observed electrocardiographic changes in six of eighteen patients (33.3 per cent), although only one showed clinical evidence of myocardial involvement. Recent evidence indicates that the disease is fatal in only a relatively small percentage of these cases, and that when recovery occurs, it is complete. In a few instances the infestation is overwhelming, and death results. Spink,[3] in 1935, was able to collect only nine cases in which the diagnosis was proved by autopsy, including one of his own, and only one case, that of Gordon, Cares, and Kaufman,[4] has been reported since that time. Because of this rarity of fatal cardiac manifestations, and because of the present interest in trichinosis, a description of a case recently studied at the Cleveland City Hospital seems justified.

CASE REPORT

History.—A. V., a white woman, 20 years of age, was admitted to the medical service of Cleveland City Hospital Jan. 10, 1939. She had been well until Dec. 23, 1938, when she first noted pain and swelling of the feet and ankles, which became so severe by the following day that she was unable to walk. Within two days there was great improvement in the condition of these joints, but she then noted pain in the right shoulder, followed by pain and swelling of the knees and elbows and severe pain in the back. During this period she had a generalized pruritic skin eruption which was said by the family physician to have been "hives." The eruption subsided within three days, and it was noted that she had fever and that her face and eyelids were swollen. She complained of pain in the abdomen and vomited on several occasions. The pain in the joints continued, as did the fever, which on one occasion reached 40.5° C. For one

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week prior to admission there was marked urinary frequency associated with some dysuria. Although the swelling of the face and eyelids subsided, she remained very ill, and on the day before admission she had a chill lasting about thirty minutes.

The past history revealed that at the age of 6 months the patient had had a generalized convulsion. Further attacks occurred at irregular intervals until she was 9 years of age. During the later seizures there was foaming at the mouth, and she was incontinent of both urine and feces. Following one of these episodes it was noted that her right eye deviated laterally, and it had remained so. An oculist who saw her at the time said that she had choroiditis. There were no convulsions after the age of 9 years, but she had been nervous and easily excited. During periods of excitement, peculiar movements of the arms and hands were noted.

After the autopsy it was learned from the family that the children frequently ate smoked, uncooked ham and that this girl had done so shortly before the onset of her illness. The other children could not definitely be said to have eaten of this ham, and they had remained well.

Physical Examination.—The patient was a well-developed, well-nourished white woman, lying quietly in bed. Her temperature was 39° C., her pulse rate 116, and her respiratory rate 20 per minute; her blood pressure was 122/76 mm. Hg. She appeared seriously ill but was rational. The skin was hot and dry. There was exotropia of the right eye, with nystagmus to the right. The pupils were equal and reacted to light and in accommodation. Both eyes were the seat of an old choroiditis, involving the macular region on the right, with patches throughout both fundi. The eyelids were not definitely swollen. Herpes labialis was present. The lungs were normal. The heart was not demonstrably enlarged. The rate was rapid, but it was regular, and no murmurs were audible. The liver and spleen were not felt. There was definite tenderness on motion of the elbows, shoulders, ankles, and knees. The left, first, metacarpophalangeal joint was swollen, red, and very tender. She was unable to sit erect without support. No subcutaneous nodules were present.

Laboratory Findings and Hospital Course.—All of the specimens of urine which were examined showed a trace of albumin, and, on one occasion, there was a trace of sugar; no cellular elements were present. The blood on admission contained 4,180,000 erythrocytes and 15,800 leucocytes per cubic millimeter; the hemoglobin was 12.5 Gm. (Sahli). A differential count of the leucocytes was reported to show 95 per cent neutrophiles, 1 per cent eosinophiles, and 4 per cent mononuclear cells. The blood Kline reaction was 2 plus with the diagnostic, and 3 plus with the exclusion, antigen, but the blood Wassermann reaction was negative. A blood culture taken on the day of admission yielded no growth.

The clinical diagnosis was acute rheumatic fever, and the oral administration of large doses of sodium salicylate with sodium bicarbonate was begun. Although the temperature began to drop slowly, the pulse rate remained elevated and she was seriously ill. The sedimentation rate of the patient's erythrocytes, ascertained by a modified Rourke-Ernstene[5] method, was 0.33 and 0.27 mm. per minute on the second and fourth hospital days, respectively (normal, 0.35 mm. per minute). Roentgenologic examination of the chest revealed no evidence of any pathologic process; the size of the heart was within normal limits. On the fourth hospital day the temperature reached 37° C., but the pulse rate was about 120, and a definite gallop rhythm appeared. Slight edema of the lower extremities and over the sacrum appeared on the sixth hospital day. She was dyspneic, and a few fine, moist râles were present at the bases of the lungs. The number of erythrocytes had dropped from the original level to 3,640,000, and the leucocytes to 10,550 per cubic millimeter, with 90 per cent neutrophiles and 1 per cent

eosinophiles. On the following day there was bleeding from the lips, gums, and nose, and purpuric spots appeared over the body. The erythrocyte count on the eighth hospital day was 2,750,000, the leucocyte count was 15,100, and the hemoglobin was 7.5 Gm. (Sahli). A differential leucocyte count showed 84 per cent neutrophiles, 16 per cent mononuclear cells, and no eosinophiles. There were 320,000 platelets per cubic millimeter, the clotting time was thirty minutes, and the clot retraction time was ninety minutes. No accurate estimation of the bleeding time was made, but blood could be obtained from a puncture wound of the finger for 45 minutes. She became more prostrated and was restless and confused. Peripheral circulatory collapse ensued, and she died on the eighth hospital day, twenty-six days after the onset of her illness.

A lumbar puncture which was done on the second hospital day revealed a clear fluid under a pressure of 8 cm. of water. The fluid contained 2 cells per cubic millimeter and no globulin. The gum mastic graph was flat, and the Wassermann reaction was negative in all dilutions.

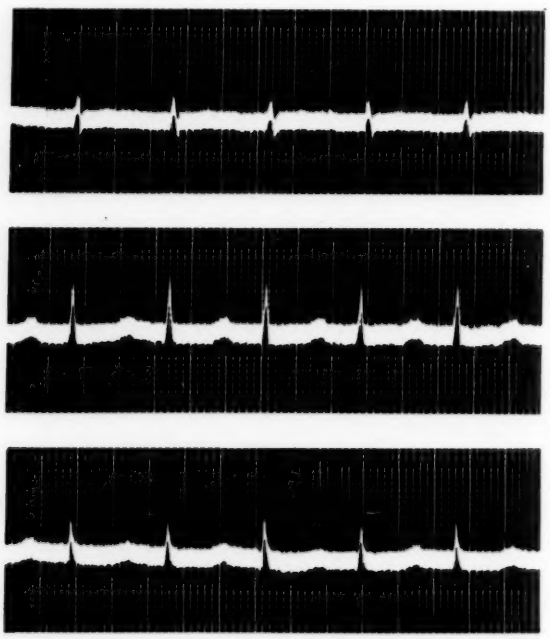

Fig. 1.—Electrocardiograms taken on the sixth hospital day, twenty-four days after the onset of the illness.

An electrocardiogram which was taken on the sixth hospital day (Fig. 1) revealed low voltage of the QRS complexes in all three conventional leads. The T-waves were barely visible; in fact, they were definitely identified in Lead II only. The P-R interval was 0.28 second.

Autopsy Findings (Autopsy No. 12522, performed by one of us, L. L. T., fourteen hours after death).—The body was that of a well-developed and well-nourished white woman, about 20 years old. Many petechiae were present in the skin, and crusts of old blood covered the nasal, labial, and gingival mucous membranes. There was edema of the subcutaneous tissues of the lower extremities and over the sacrum. The skeletal muscles were a deep reddish brown and of normal texture and consistency. Except for a few small hemorrhages in the pectoral muscles, they showed nothing unusual. The right and left

pleural spaces and the peritoneal cavity contained 250, 300, and 250 c.c., respectively, of clear, straw-colored fluid. All serous surfaces were smooth and glistening.

The heart weighed 210 Gm. and was dilated. There were a few small hemorrhages in the subepicardial fat, but the surface was smooth. The walls of the right and left ventricles measured 3 and 9 mm., respectively, in thickness. The myocardium was a pale reddish brown, dull, and flabby. There was no fibrosis, and no mural hemorrhages were seen. The entire endocardium was smooth, and the valve leaflets were thin and delicate. The coronary arteries were normally distributed and showed no abnormalities.

There were edema of the lungs and severe passive hyperemia of all viscera. The liver weighed 1,470 Gm.; the cut surface bulged and was soft, dull, and pale yellowish brown. The spleen weighed 285 Gm. and was the seat of severe, acute hyperplasia. There was severe hyperemia of the entire gastrointestinal tract, and there were numerous small hemorrhages in the mucosa of the esophagus, stomach, and small intestine, and also in the mesentery and mesocolon. The brain was normal.

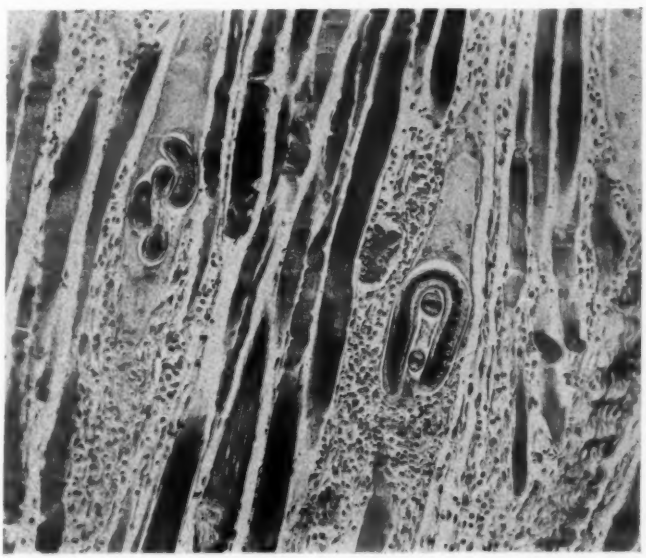

Fig. 2.—Pectoral muscle, showing partially encysted parasites. (Hematoxylin-eosin ×100.)

Microscopic examination of the pectoral muscles revealed numerous larvae between and within swollen, hyalinized muscle fibers (Fig. 2). In some of the sections as many as four parasites were present in a single low-power (×100) field. The organisms were surrounded by syncytial masses containing large, round, coarsely vesicular nuclei, but there was no perifocal fibrosis or calcification. Collars composed of eosinophiles, lymphocytes, neutrophiles, large mononuclear cells, and a few plasma cells were present about the encysted larvae. Similar cells diffusely infiltrated the interstitial connective tissue, and the muscle cells were swollen and pale.

Sections through all chambers of the heart showed severe fragmentation of the muscle fibers, with swelling of some and shrinkage of others. The interstitial connective tissue was diffusely sprinkled with inflammatory cells, and, as in the skeletal muscle, numerous collections of eosinophiles, neutrophiles,

lymphocytes, and a few large mononuclear and plasma cells were scattered throughout the myocardium in association with focal necrosis of the muscle fibers (Fig. 3). These foci were rarely found in the connective tissue septa and bore no relation to the blood vessels. In the centers of a few there were small syncytial masses containing from two to three large vesicular nuclei, and several contained half-coiled embryos (Fig. 4). The endocardium and epicardium were normal in all sections. A post-mortem culture of the heart's blood yielded no growth, and bacterial stains of the myocardium revealed no organisms.

In the muscular coats of the esophagus and small intestine, in the wall of the urinary bladder, and deep in the substance of the myometrium, there were a few tiny foci of necrosis associated with an infiltration of lymphocytes, eosinophiles, and a few large mononuclear cells. These lesions were identical with those present in the myocardium, but no parasites were found. There were severe passive hyperemia of the lungs and abdominal viscera, fatty degeneration of the liver, acute hyperplasia of the spleen, and severe cloudy swelling of the kidneys.

As the true nature of the disease was not suspected at the time the autopsy was performed, no fresh muscle was taken for analysis. Williams,[6] in 1901, pointed out that formalin-fixed tissue could be satisfactorily examined by a compression technique, but we found no report concerning the digestion of such tissue with artificial gastric juice. Using fixed and unfixed muscle from another body, it was discovered that washed, formalin-fixed tissues could be digested if the incubation was continued for seventy-two hours. Pectoral muscle from this patient which had been preserved in 10 per cent formalin for two weeks was digested, and about 250 larvae were obtained from 10 Gm. of tissue. Except for the blocks saved for microscopic study, the entire heart, which also had been fixed, was similarly examined, but no parasites were found. It is regrettable that the efficiency of the method could not have been controlled with fresh muscle; it appears, however, that this technique may be employed satisfactorily in the diagnosis of trichinosis when fresh material is not available.

COMMENT

Mistaking trichinosis of the myocardium for rheumatic myocarditis, even in the absence of clinical evidence of endocardial or pericardial involvement, has not, to our knowledge, been reported previously. Considering the comparative rarity of trichinous myocarditis and the fact that it is usually associated with severe myositis, eosinophilia, and facial and palpebral edema, this is not surprising. In this case, a history suggesting acute inflammatory arthritis, the presence of myocardial disease, as shown by tachycardia which was out of proportion to the fever, gallop rhythm, electrocardiographic changes, and progressive congestive failure, together with the associated leucocytosis, progressive anemia, and purpura, constituted weighty evidence for the diagnosis of acute rheumatic fever. In retrospect it would appear that too little attention had been paid to the fact that the sedimentation rate was normal on two occasions, and to the history of swelling of the face and eyelids. It is recognized, however, that the sedimentation rate remains normal in a small percentage of cases of acute rheumatic fever; Massell and Jones[7] found that it was within

normal limits in twenty-one of ninety-seven patients showing clinical evidence of active rheumatic fever. They also found that it was normal in six of fourteen cases in which there was a prolongation of the P-R interval caused by rheumatic heart disease. Westergren[8] has pointed out that congestive failure may lower the sedimentation rate, and, since failure was obviously present in this case, it was con-

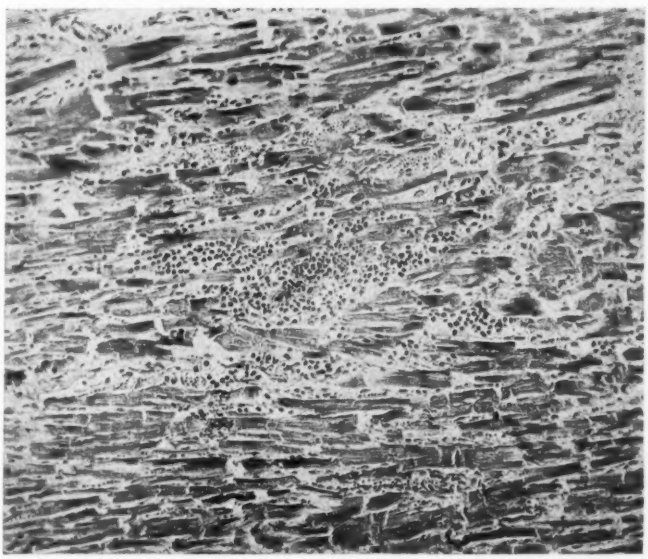

Fig. 3.—Myocardium, showing focal character of the inflammatory exudate. (Hematoxylin-eosin ×100)

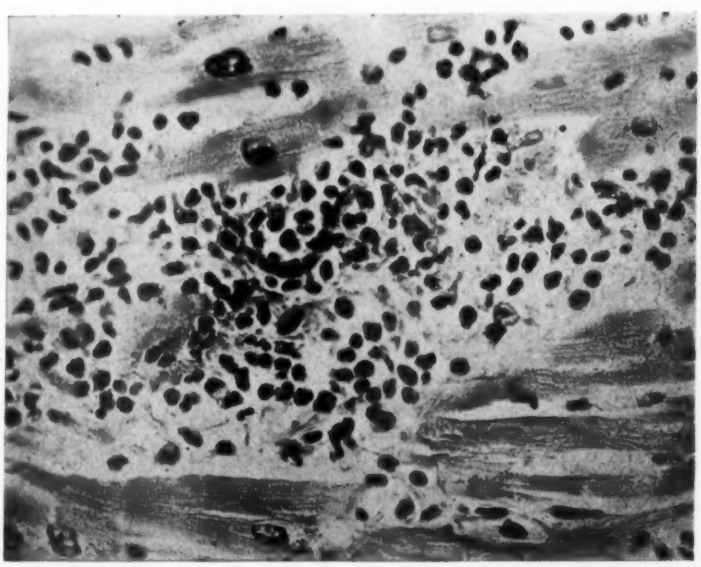

Fig. 4.—Myocardial lesion containing embryo. (Hematoxylin-esosin ×550)

sidered responsible for the normal rate. As for the swelling of the face, this was not present at the time of admission and was thought to have been caused by urticaria.

Eosinophilia, the one manifestation which more frequently than any other calls attention to the possibility of trichinosis, was absent in this case. Tyzzer[9] states that eosinophilia is often absent in the presence of an intercurrent infection, and Faust[10] writes that "although it is a relatively uncommon situation, it is well recognized that the prognosis in a case of heavy trichinella infection with little or no eosinophilic response is invariably grave and usually fatal." Reifenstein and his associates,[11] on the basis of an extensive review of the literature, offer further support of this statement. Pepper,[12] Spink,[3] Gordon, Cares, and Kaufman,[4] and others have also noted the absence of eosinophilia in severe and fatal cases. Although there was no demonstrable intercurrent disease in this case, it illustrates the point made by these workers. It is noteworthy that, despite the absence of eosinophilia in the circulating blood, eosinophiles constituted an important part of the exudate in the skeletal and cardiac muscles, which suggests that the tissue demands equalled or exceeded the rate of production and prevented accumulation in the blood.

The electrocardiographic changes attributed to trichinosis of the myocardium have been described by Pardee,[13] Spink,[3] Master and Jaffe,[14] Cushing,[15] and Beecher and Amidon,[2] and they include initial flattening or inversion of the T-wave, especially in Lead II (the wave subsequently becomes upright), low amplitude of the QRS complex, and intraventricular block. The changes in this case conform to those described.

The characteristic microscopic features of trichinosis of the myocardium, which were present without exception in this case, are adequately described in the existing reports. They consist of a focal, acute myocarditis, with necrosis of muscle fibers and an infiltration of inflammatory cells, including many eosinophiles. The necrosis of the muscle cells, the character of the infiltrate, with its many eosinophiles and relatively few large mononuclear cells, and its lack of proximity to blood vessels distinguish this disease from rheumatic and other forms of acute myocarditis.

An adequate explanation for the scarcity of larvae and their failure to encyst in the myocardium is difficult to find. Because he failed to find the parasites, Simmonds[16] contended that the cardiopathy is the result of specific intoxication, not of true infection. The presence of larvae in the histologic preparations studied by Zenker,[1] Frothingham,[17] Prym,[18] Horlick and Bicknell,[19] and ourselves and their recovery by Spink[3] after digestion of the heart muscle discredit this hypothesis. Furthermore, Dunlap and Weller[20] were able to find embryos in the myocardium of experimentally infected white mice as early as five days after the parasites were ingested. In animals

which were allowed to live beyond the period of active migration, however, they failed to find myocarditis, although there were still many incompletely encysted parasites in the skeletal muscles. They conclude from their experiments that "the presence of larvae in the myocardium and their active migration, and not a blood-borne toxic substance, produces the characteristic myocarditis." They state that it is not clear what properties inherent in the cardiac muscle prevent the encystment of larvae. In our case, it is probable that the prolonged treatment necessary to digest the fixed muscle resulted in complete destruction of the already degenerating trichinae.

SUMMARY

A rapidly fatal case of trichinosis, with myocardial involvement, which was mistaken for acute rheumatic fever, is reported. Trichinae were present in sections of skeletal and cardiac muscle and were recovered from formalin-fixed skeletal muscle, but not from fixed myocardium by digestion.

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PAROXYSMAL VENTRICULAR TACHYCARDIA

With Report of an Unusual Case

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WE HAVE recently had under our care a man who had an attack of ventricular tachycardia which lasted without intermission for twenty-three days; he had had a similar attack eight months previously which may have been without intermission for a considerably longer period. This last attack was controlled only by giving quinidine sulfate intravenously in an unusually large dose, and with a most dramatic effect. These facts, together with the variety of other methods of therapy employed, seem to justify the following report:

CASE REPORT

B. M., a Dane, 41 years old, a carpetlayer, was first seen on Aug. 11, 1938, at which time he complained chiefly of tachycardia and shortness of breath.

The past history revealed that during childhood he had suffered from scarlet fever and diphtheria, and that in 1930 a mastoidectomy had been performed for acute mastoiditis. There was no history of rheumatic fever.

The present illness had begun about three months previously, when, while at a "party," he suddenly developed an extremely rapid pulse rate, with, however, no other symptoms. The following day he was admitted to another hospital, where he remained for five weeks, during which time he was given, at various times, large doses of digitalis, sedatives, and quinidine, orally. The pulse rate on no occasion was below 110 beats to the minute, and the patient noticed a gradual increase in dyspnea and loss of strength. By Aug. 4, 1938, he had become so discouraged that he was prevailed upon to discontinue the services of his physician and seek aid from Christian Science. By August 8 the pulse had again become extremely rapid, the dyspnea had increased markedly, a dry, hacking cough had developed, and the patient was unable to sleep.

On Aug. 11, 1938, examination revealed a pale, restless man who was "scared to death" and showed moderate dyspnea when propped up in bed. There was no cyanosis. His state of nutrition was fair. All of his teeth had been extracted; the tonsils were present, but not obviously infected. An extremely rapid jugular pulsation was noted; its rate was the same as that of the heartbeat. The thyroid was normal. The peripheral arteries showed no evidence of sclerosis; the radial pulse was scarcely perceptible. The blood pressure was recorded as 95/75 in both arms. The heart appeared to be grossly enlarged to the left; the area of cardiac dullness extended to the left anterior axillary line. The beating was regular, and no murmurs were heard. The rate was counted many times and found to be from 180 to 200 beats to the minute.

Examination of the lungs revealed impaired resonance posteriorly, with inspiratory râles over the lower half of both lungs. The liver was enlarged and acutely tender; its lower edge was palpable in the right midclavicular line at the level of the umbilicus. There was no free fluid in the abdomen, nor were any other solid viscera palpable. There was no edema of the legs, genitals, or back. Rectal examination and examination of the central nervous system showed nothing abnormal.

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The diagnosis was paroxysmal tachycardia, with impending congestive heart failure.

The patient was given ¼ grain of morphine sulfate hypodermically and 10 grains of quinidine sulfate orally and was transferred immediately to the Vancouver General Hospital.

Routine laboratory studies of the urine and blood, including the Kahn test, showed nothing abnormal.

The electrocardiogram showed ventricular tachycardia (Fig. 1). The patient was given 10 grains of quinidine sulfate every hour for four hours. A solution of 10 grains of quinidine sulfate to 100 c.c. of normal saline was prepared, and several hours after admission this solution was given intravenously. When approximately 50 c.c. (5 grains) had been administered, the patient vomited suddenly and violently, and the injection was stopped. The heart rate dropped to 160 per minute. The following morning 150 c.c. of a similar quinidine sulfate solution were given intravenously. Severe vomiting occurred again, when ap-

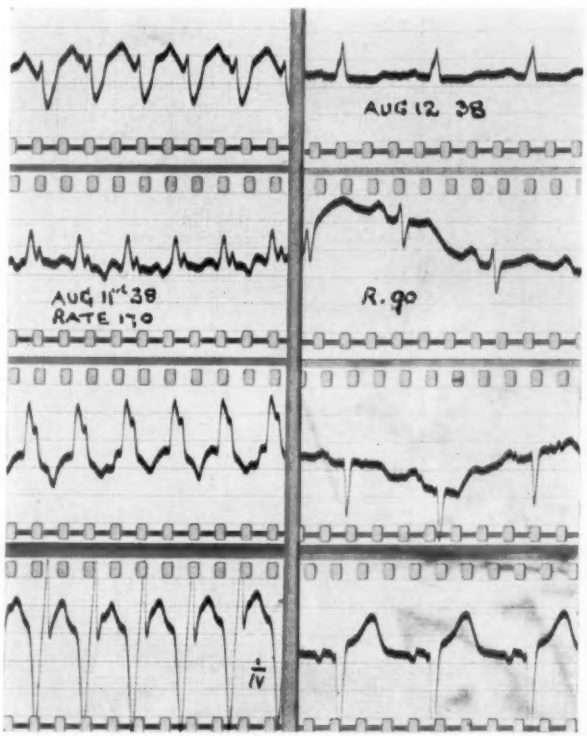

Fig. 1. Fig. 2.

Fig. 1.—Aug. 11, 1938. First attack of ventricular tachycardia. Rate 170.
Fig. 2.—Aug. 12, 1938. Sinus rhythm after administration of 15 grains of quinidine sulfate intravenously. Rate 90.

proximately 15 grains of quinidine had been administered. The heart rate, however, suddenly dropped to 96. An electrocardiogram which was taken shortly afterward (Fig. 2) showed normal sinus rhythm. Quinidine sulfate was thereafter administered orally in doses of 5 grains every four hours, and this was gradually reduced to 5 grains three times a day. He was discharged August 15.

On August 17, his pulse rate was 80, and his blood pressure was 100/70. There was slight edema of the ankles, and the liver was just palpable. All signs of congestive failure rapidly disappeared, and during the remainder of 1938 he took small

daily doses of quinidine and remained quite well. During December, however, frequent extrasystoles made their appearance, and in January he had two attacks of tachycardia which lasted but a few minutes. On February 8, frequent extrasystoles were noted during examination, and these continued during March and April. Throughout this period quinidine sulfate was continued in doses of 5 grains three or four times a day.

On April 24, at 1 A.M., tachycardia developed suddenly, and the patient took 15 grains of quinidine sulfate and repeated it in two hours. At 9 A.M. the rate was 132, and he was immediately hospitalized (Fig. 3). Twenty grains of quinidine sulfate in 100 c.c. of physiologic saline were given intravenously, with no reduction in the heart rate. This was repeated in nine hours and caused a severe reaction, but the pulse rate fell only to 100. The oral administration of quinidine sulfate was resumed. He received 10 grains every four hours until the morning of April 27, when he was again given 20 grains intravenously, this time in 100 c.c. of 5 per cent glucose solution. No further oral medication was given, and in twenty-four hours' time the above dose was repeated. On April 28 quinidine was discontinued, and on April 29, 3 grains of digitalis were administered every four

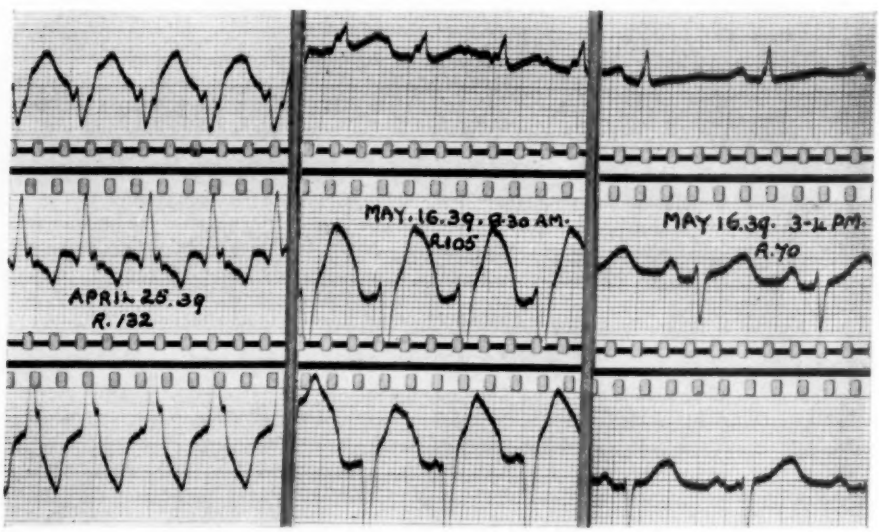

Fig. 3. Fig. 4. Fig. 5.

Fig. 3.—April 25, 1939. Second attack of ventricular tachycardia. Note similarity to Fig. 1. Rate 132.

Fig. 4.—May 16, 1939, at 8:30 A.M. Immediately after intravenous administration of 40 grains of quinidine sulfate. Note change to tachycardia of supraventricular origin. Rate 105.

Fig. 5.—May 16, 1939, six hours after the electrocardiogram of Fig. 4. Sinus rhythm. Rate 70.

hours. Within twelve hours the pulse rate rose to about 190, and the patient became orthopneic, cyanotic, and very worried; morphine relieved these symptoms in part. By the time quinidine had been withheld for twenty-four hours, his condition was extremely bad. Twenty grains of quinidine sulfate in 100 c.c. of 5 per cent glucose solution, given intravenously, reduced the tachycardia to 120 beats per minute, with very marked improvement in the patient's general condition. Two hours later 1 mg. of prostigmin was given, with no subjective or objective effect. Later, oral administration of quinidine was resumed, with 10-grain doses every four hours. On May 1, 25 mg. of mecholyl were given, without

effect. Twenty 5-grain capsules of quinidine were then left at the patient's bedside, and he was urged to take as many of these as possible in each twenty-four-hour period. He was able to take only eighteen of these, or 90 grains of quinidine. By this method it was possible to keep the heart rate around 120, and he was fairly comfortable when propped up in bed.

On May 3, 0.25 mg. of ergotamine tartrate was given intravenously, with no effect on the tachycardia. Within a few hours phlebitis developed in the vein into which this had been injected, although not at the site of injection. On May 6, 20 grains of quinidine sulfate in 5 per cent glucose solution were again administered intravenously, with a reduction of the pulse rate from 140 to 108. On May 8, 10 c.c. of a 20 per cent solution of magnesium sulfate were given intravenously, with no success. Phlebitis developed in the other arm.

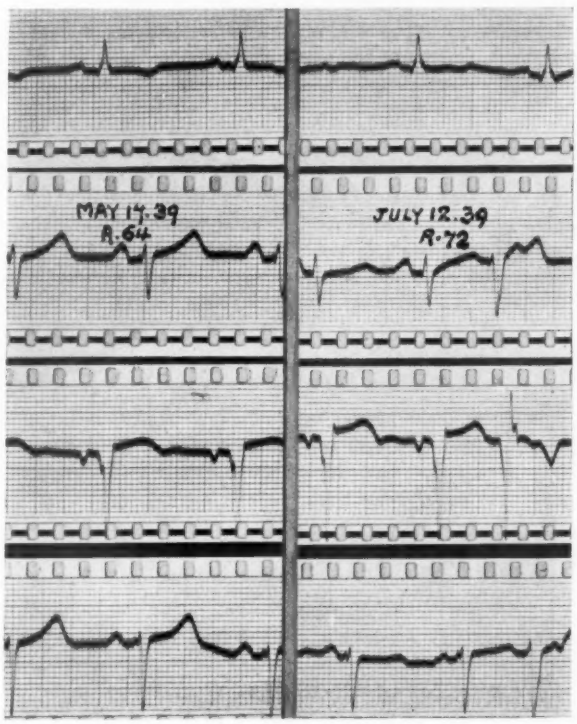

Fig. 6. Fig. 7.

Fig. 6.—May 17, 1939. Sinus rhythm. Note inversion of P_3, and signs of myocardial involvement. Rate 68.

Fig. 7.—July 12, 1939. Sinus rhythm. Note frequent extrasystoles. Rate 65-75.

On the morning of May 11 quinidine was stopped, and within ten hours the heart rate had risen to about 180. Twenty-five milligrams of mecholyl were then given subcutaneously, with no effect, and this was followed by 20 grains of quinidine, during the administration of which the rate dropped to 130. The drug was then resumed orally. On May 13, 0.5 mg. of ergotamine tartrate was again tried, following which a flare-up in his phlebitis occurred. Again, on May 14, 20 grains of quinidine sulfate were given intravenously, and the pulse rate fell to 96, where it remained for about forty-five minutes. During all of this time electrocardiograms were taken every two or three days, and all showed persistence of the ventricular tachycardia.

Finally, on May 16, when the patience of both doctor and patient had become almost exhausted, and the ill effect of the persisting tachycardia was becoming

apparent, he was given 40 grains of quinidine sulfate intravenously. The usual symptoms were observed by the patient; after from 25 to 30 grains had been injected, he vomited. A distinct change in the character of the heart sounds was noted, the patient became unconscious, and a violent epileptiform convulsion occurred. This convulsion lasted about one minute. Consciousness was not regained for about fifteen minutes, during which time the patient was carefully watched and coramine was administered. The heart rate at the onset of this injection was 176, and one hour later it was 114. When he awakened, the patient immediately recognized the fact that normal rhythm had returned, and his excitement was so great that opiates had to be used to keep him quiet. An electrocardiogram taken immediately after this large injection, while the patient was still unconscious, revealed a complete change of rhythm, with a rate of 105 (Fig. 4). The tachycardia at this time was supraventricular in origin, but within six hours this changed spontaneously to sinus rhythm (Fig. 5). The quinidine was thereafter administered in four 5-grain doses daily, and when he was discharged, May 23, he showed no evidence of cardiac failure. Extrasystoles have been present intermittently since that time, but otherwise he has been quite well (Figs. 6 and 7).

An analysis of this case report brings to light certain features which have been described before, and others which are less well known. The sudden onset is one of the characteristics of the tachycardia, but it is no more characteristic than sudden cessation. In our case, however, there was a gradual reduction in the cardiac rate from 176 per minute at the start of the last intravenous injection to 96 two hours later, and during this time, before sinus rhythm was established, supraventricular tachycardia was present for an indeterminate time. To our knowledge, no patient who recovered has shown such a transformation before the resumption of normal rhythm.

All of the usual methods of vagal stimulation—mechanical, such as carotid sinus pressure and pressure on the eyeballs, and chemical, produced by mecholyl, ergotamine, and prostigmin—were tried with little hope and no success. One or more of these measures have often succeeded in terminating supraventricular tachycardia, but not ventricular tachycardia.

Many times during the course of this illness, quinidine, administered orally or intravenously, slowed the cardiac rate without altering the abnormal rhythm. The patient was a highly intelligent man, and his immediate request, when the rate rose above 150 and dyspnea was increased, was for more quinidine "to slow it if we can't stop it." Time and again the rate was reduced 30 to 50 beats per minute by larger doses orally, or an intravenous injection, with coincident relief of symptoms, but without abolishing the abnormal rhythm. This quinidine effect has been noted before.[1]

One of the characteristics of ventricular tachycardia, first pointed out by Strong and Levine,[2] in 1923, is the slight irregularity which can be noted on careful auscultation, which is in contrast to the absolute regularity of auricular tachycardia. This was true in our case. Furthermore, alterations in the character of the heart sounds at the apex were

not uncommon, and especially was this evident from minute to minute during the intravenous injections of quinidine. Digitalis was an unqualified failure and, in fact, made the condition much worse. Strophanthin was not used.

Ventricular tachycardia usually occurs in association with organic heart disease, and we believe that the latter is present in our case (Figs. 2, 6, and 7). The significance of his frequent extrasystoles is an open question. We are also aware of the fact that quinidine may, in odd instances, incite ventricular tachycardia, but without the drug his extrasystoles are much more frequent and disturbing, and we cannot help feeling that complete withdrawal of the drug would increase his liability to another attack of tachycardia.

In addition to being an excellent example of the therapeutic value of quinidine, this case also afforded ample opportunity for study of the toxicity of the drug. With large doses orally, the patient would complain of a sensation of "sand" in his eyes, followed by blurring of vision, tinnitus, vertigo, and nausea. Vomiting did not occur when the drug was given orally, even when from 80 to 90 grains were taken in twenty-four hours. When it was given intravenously, the above symptoms appeared rapidly, before 10 grains were administered, and violent vomiting ensued after from 15 to 30 grains had been given. The blood pressure tended to rise above the low level associated with the tachycardia. During the final injection, after 30 grains had been given, the patient complained of a sensation of burning over his entire body which persisted for a few minutes. After receiving 40 grains, he lost consciousness, and a severe generalized epileptiform convulsion occurred. In from ten to fifteen minutes, when consciousness was regained, tinnitus, vertigo, and headache were present, and diminished acuity of hearing persisted for three hours.

SUMMARY

An unusual case of paroxysmal ventricular tachycardia is reported. The attack lasted twenty-three days, without intermission. The possibility that the patient had suffered previously from a much longer attack is to be considered.

The therapy is outlined. Many therapeutic agents were used, but the only one of value was quinidine; this was effective only when given intravenously in the large amount of 40 grains. We believe, however, that this route of administration should be used only in an emergency and after oral administration has failed.

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1. Salley, S. M.: An Unusual Atropine Effect on Ventricular Tachycardia, Am. J. Med. Sc. **183**: 456, 1932.
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CONGENITALLY DOUBLE LEFT AURICLE

Report of a Case

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CONGENITAL cardiac anomalies are reasonably common, but the so-called double left auricle is extremely rare. Palmer,[1] in 1930, collected ten cases from the literature and added the report of an eleventh. We have recently seen a patient who belongs in this group, and herewith present the twelfth such case.

CASE REPORT

H. Y., an 18-year-old, single, white man, was admitted to the medical wards of the Hillman Hospital, Birmingham, Ala., Dec. 21, 1938. The history was given by both the patient and his mother.

Complaint.—He complained of cough, hemoptysis, dyspnea, and undue fatigue on exertion.

Family History.—His father had died at the age of 28 of heart disease of undetermined nature. The mother was living and well, and there were no siblings.

Past History.—Apparently he had been a normal baby, and had developed normally. He had had uneventful attacks of whooping cough, measles, and mumps during childhood.

At the age of 7, eleven years before admission to the hospital, he was seen by a physician because of precordial pain, and it was said that he had "leakage of the heart."

At the age of 14, the appendix was removed.

At the age of 15, because of recurrent tonsillitis for several years, the tonsils were removed.

Prior to the present illness he had been an active boy, and did not feel that anything was wrong with him. He had played football, though never for a whole game. There was no history of growing pains, joint pain, rheumatism, or of any symptom other than those enumerated.

At the age of 18, in March, 1938, nine months before admission to the hospital, he was examined and accepted for the United States Navy. He was told that he was in perfect health after what he described as a rather complete physical examination. He became ill before he was called for service.

Present Illness.—In April, 1938, eight months before admission to the hospital, he began to note undue fatigue on ordinary exertion. It was accompanied by dizziness and blurred vision. In late summer or early fall, he began to have palpitation on exertion. In the late fall he had a "cold," with considerable cough and hemoptysis with the severest coughing. After mid-November, hemoptysis occurred daily. For an indefinite period there had been pain under the right costal margin and a poor appetite. His weight had declined from 160 to 130 pounds in six months. There had been no other symptoms.

Examination.—The patient was orthopneic, but was fairly comfortable. He coughed occasionally, expectorating frothy, bloodtinged sputum. He was not cyanotic. His temperature was normal.

There were many crepitant râles at the bases of both lungs, without other abnormal physical signs in the lungs. Respirations were 24 to the minute.

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The heart seemed enlarged to percussion. There was a diffuse precordial impulse which was most definite to the left of the sternum in the fifth intercostal space. The pulmonic second sound was greatly accentuated. There was a slightly rough, blowing murmur which was heard over the entire precordium during the last half of diastole. It was quite loud at its maximal point in the fourth intercostal space, just to the left of the sternum, and it was transmitted best upward along the left sternal margin. It was barely audible at the apex. There were no systolic murmur and no thrill. The heart rate was 120, and the rhythm normal. The blood pressure was 144/78.

The edge of the liver was palpable five centimeters below the right costal margin. It was smooth and tender. There was no ascites or edema. There was no clubbing of the fingers. There were no other abnormal physical findings.

The blood Kline reaction was negative. The hemoglobin was 74 per cent, and the erythrocyte count 4,610,000. The leucocyte count was 13,800, with 74 per cent neutrophiles and 24 per cent lymphocytes. The urine contained a few erythrocytes on one examination, and a trace of albumin on another, but was otherwise normal. A blood culture remained sterile.

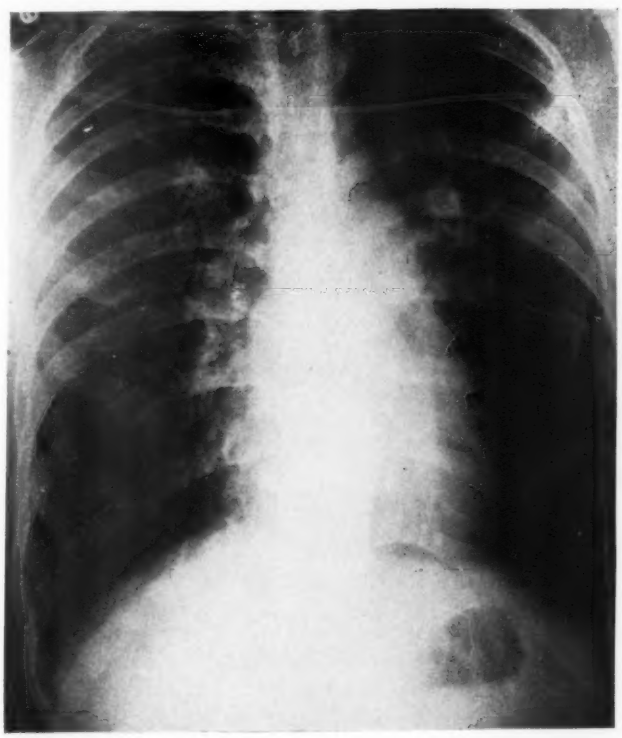

Fig. 1.

A teleoroentgenogram (Fig. 1) showed no enlargement of the heart. There was slight bulging of the cardiac outline in the region of the left auricle.

The electrocardiogram made on Dec. 31 (Fig. 2) showed marked right ventricular predominance, and inversion of P_4, T_2, and T_3. There was slight notching at the summit of R_3, but no other abnormality.

Hospital Course.—With rest in bed, digitalis, and phenobarbital he became more comfortable and less orthopneic. He stopped coughing. He did not seem acutely

ill, and, after four days in the hospital, was allowed to go home for Christmas day. He was transported by automobile, spent the day in bed, and then returned to the hospital as planned. There were no apparent ill effects.

On December 31 he seemed to be in still better condition. He was transported several blocks by automobile. There was only slight exertion, but afterward he seemed rather tired. Later that day, the temperature rose to 102° F., and, until his death on the second day thereafter, it ranged from 100.4 to 103.6° F. There were a few moist râles at the bases of the lungs. The character of the murmur did not change. On January 2 he became very dyspneic, coughed frequently, and expectorated bloody material. He died Jan. 2, 1939, twelve days after admission.

Post-Mortem Examination.—The heart (Fig. 3) weighed 390 grams. It was enlarged chiefly on the right side. The left auricle was small and thickened. When the auricle was opened there appeared to be only a small slit, not even admitting the finger tip, between left auricle and ventricle. This, and the funnel shape of what was apparently the floor of the auricle, gave the appearance of marked mitral stenosis.

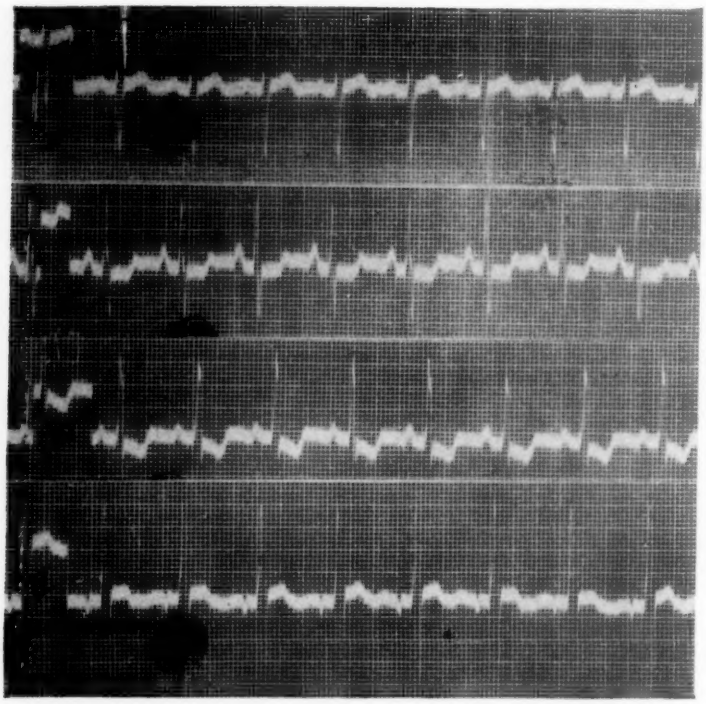

Fig. 2.

When the rest of the heart was opened it was seen that the mitral valve was normal, but that immediately above it there was a complete diaphragm rising from the wall of the left auricle in a circular fashion, dividing it into a larger upper posterior, and a smaller lower anterior, portion. It joined the interauricular septum above the closed foramen ovale. In this anomalous diaphragm there was the slit-like opening previously noted, which measured 0.5 by 0.2 cm. To the left of, and posterior to, it there was another, similar slit, measuring 0.5 by 0.3 cm. In the photograph (Fig. 3), probes are seen passing through these openings. The diaphragm itself was fairly thick and gray-white, and there were a few heavy bands passing from its under surface to the wall of the auricle.

Microscopic examination showed that the diaphragm was made up of cardiac muscle fibers separated by fibrous tissue. Muscle predominated at the periphery, but in the center it consisted chiefly of fibrous tissue. Both surfaces were covered by endothelium. The wall of the left auricle was rough, a dull gray-white in color, and hypertrophied (the wall measured 0.4 cm. in thickness above the diaphragm; below the diaphragm it measured 0.2 cm.).

The right ventricular wall was moderately thickened, measuring 0.6 cm. The left ventricle, right auricle, and all valves were normal except for an irregular, subendocardial hemorrhage on the right cusp of the pulmonary valve. The coronary vessels were normal.

The lungs showed bronchopneumonia, in addition to considerable congestion and edema. There was congestion of the liver, spleen, kidneys, and intestinal mucosa.

There were no other abnormalities.

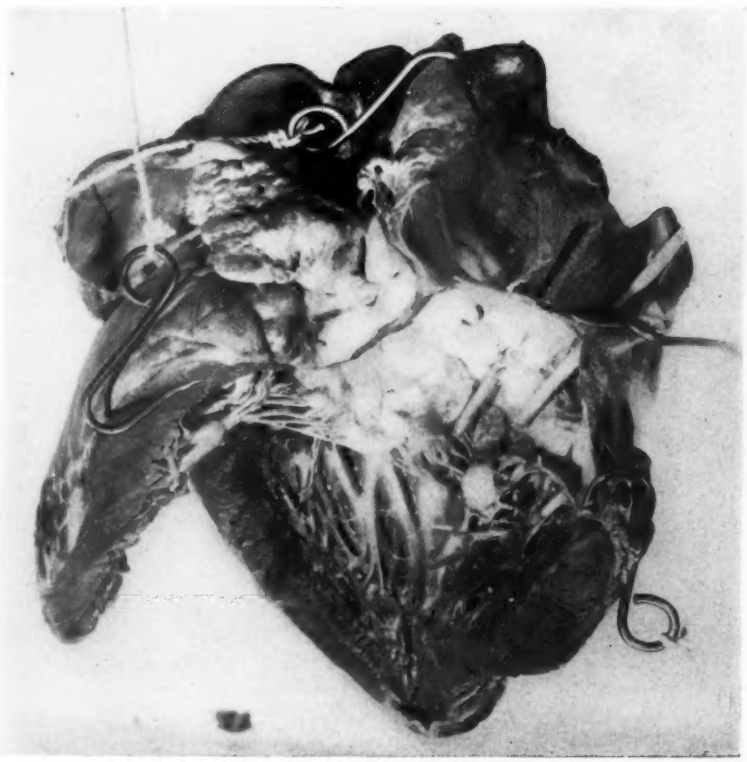

Fig. 3.—The heart at autopsy, showing the cut edge of the anomalous diaphragm across the left auricle, which has been opened. The closed foramen ovale can be seen below the diaphragm to the left of the probes in the two slit-like openings in the diaphragm.

COMMENT

No reason was found for the apparent absence of the very loud murmur less than a year before death. As the lesion was of a type thought to be congenital, and as there was no history of disease that might have resulted in cardiac damage, we can but conclude that the

murmur was simply not heard at the examination in April, 1938. In December, it was scarcely audible at the apex. It seems entirely probable that the lesion and murmur had been present since birth.

The diaphragm across the left auricle, with its very small openings, produced an effect comparable to that of an advanced mitral stenosis. There were pulmonary congestion with left auricular hypertrophy above the obstructing diaphragm, right ventricular hypertrophy, and heart failure. It is felt that these produced his presenting symptoms, and that these and bronchopneumonia caused death. No reason, however, was found for the progression of symptoms that brought him to the hospital.

We can add nothing to the comments on etiology made by Palmer.[1] He suggested that the upper chamber, that above the anomalous diaphragm, does not represent auricle, but rather the dilated end of the fetal, common pulmonary vein. The space below the membrane would then be, in reality, the whole auricle. The relation of the foramen ovale to these chambers adds to this hypothesis. Palmer also suggested the possibility that the diaphragm may have resulted from fetal endocarditis, or from the organization of a thrombus. Our data neither confirm nor deny any of these hypotheses.

REFERENCE

1. Palmer, George A.: Cardiac Anomaly (so-called Double Left Auricle), Am. Heart J. 6: 230, 1930.

Department of Reviews and Abstracts

Selected Abstracts

Wright, G. M., and Phelps, Kenton: A Comparison of Procedures for Increasing Blood Flow to Limbs Using an Improved Optical Plethysmograph. J. Clin. Investigation **19**: 273, 1940.

Despite many advantages of the Hewlett-Van Zwaluwenburg plethysmographic method for determining blood flow in the limbs, this procedure—and even more its modification by subsequent workers—has a number of hidden faults which lead to inaccuracies in the estimation of flow under different conditions. Among these are: the yielding diaphragm surrounding the limb and closing the plethysmograph, displacement of fluid into the plethysmograph by inflation of the collecting cuff, and lack of sensitivity of the entire apparatus.

A boot plethysmograph is described which is easy to apply and calibrate, the open end of which is sealed around the leg without constriction by the use of plaster of Paris and Unna paste, and which is comfortable for prolonged periods of study. The apparatus is connected to a Frank segment capsule giving the entire system frequencies up to 100 per second.

To obviate the artefacts incurred through displacement of fluid into the plethysmograph by the inflated cuff, an arrangement of stopcocks is provided by which the collecting cuff is inflated while the plethysmograph and recording capsule remain open to the atmosphere; but exactly one second later it is automatically closed and the volume changes are recorded. The rise of a full pulse beat starting exactly 1.6 seconds after inflation is used to measure the net flow per cycle. From this the volume flow per minute per 100 c.c. of leg substance is calculated in the conventional manner.

The phasic arterial blood flow of the leg recorded in this way for normal subjects at rest in a warm room (28° to 30° C.) shows three distinct variations during each cycle: (1) a rapid systolic forward flow, (2) a slower, smaller, and variable systolic backflow, (3) a slow forward flow during diastole. The net arterial inflow depends not only on 1 plus 3 but also upon the amount subtracted by 2. All of these vary under different circumstances. Since only the amplitude (phase 1 above) of the pulse volume is recorded by plethysmographs or oscillometers, these methods give no quantitative estimate of changes in volume flow, and under some conditions they do not even show the correct directional changes.

The resting flow determined by our procedure remains constant within approximately 6 per cent of the mean during repeated determinations within an hour. It varies greatly in different individuals or in the same individual from day to day unless strictly basal conditions are observed.

A study of various procedures suggested for promoting a maximal blood flow in the leg shows that direct application of heat and sciatic nerve block are the most efficacious. Application of heat to both upper extremities (reflex heat) produces an effect only about one-half as great. We were unable to detect any increase in blood flow following effective spinal anesthesia or sacral diathermy.

Other procedures which affect heart rate or blood pressure significantly influence blood flow in a variable manner. Amyl nitrite, for example, increases the amplitude of oscillations but often causes an actual decrease in volume flow.

AUTHORS.

Burchell, Howard B.: Adjustments in Coronary Circulation After Experimental Coronary Occlusion. Arch. Int. Med. **65**: 240, 1940.

The anatomy of the coronary arteries in the dog is reviewed, with emphasis on the presence of a large septal branch and the free anastomoses between the ventricular and auricular coronary branches. Extracardiac communications on the great vessels at the base of the heart have been demonstrated without difficulty.

Constriction of the main coronary vessels to an estimated 35 to 60 per cent of their diameter over lengths of 7 mm. caused no disability if the animals recovered from the immediate effects of the operations. Ligation of severely constricted vessels could frequently be made without the production of infarction. Complete occlusion without the production of infarction has been accomplished by constricting metal collars which were loosely anchored to the wall of the chest.

By these methods it has been possible to occlude the three main coronary branches in the dog without the production of infarction or demonstrable cardiac disability. Re-establishment of the circulation has occurred from the first branches of the coronary stems and by enlargement of pre-existing collateral channels.

So far as these studies on coronary occlusion in dogs are concerned, the role played by vascular channels in pericardial adhesions in supplying blood to the myocardium has been minimal or nonexistent. The possibility that the small vascular connections between a graft and the heart might develop to a functioning value cannot be denied, but in the experiments seemingly favorable to such a result it has not occurred.

AUTHOR.

Stokvis, Von Berthold: Automatic, Unbloody Registration of the Blood Pressure in Man. Cardiologia **4**: 75, 1940.

After a review of literature about the uninterrupted measuring of blood pressure, a method is described for the uninterrupted, automatic, unbloody registration of the systolic and diastolic blood pressure in man.

AUTHOR.

Groedel, F. M.: Topography and Time of Appearance of the Action-Potential of the Heart on the Anterior and Posterior Chest Wall in Young Healthy Persons. Cardiologia **4**: 1, 1940.

The different forms of the chest electrocardiographs obtained by leading from different areas of the anterior and posterior chest wall, to a place distant to the heart, are explained on the basis of the examinations of two young persons with healthy hearts.

It is shown that there are three different types of chest electrocardiographs, the right (d.-electrocardiograph), the left (s.-electrocardiograph), and the transitional forms. It is demonstrated on which areas of the anterior and posterior chest wall these three electrocardiograph forms are to be found. The potential changes at the different places on the chest wall are explained in detail, and the time differences in the appearances of these potential undulations at the different places are recorded.

AUTHOR.

Stewart, Harold J., and Bailey, Robert L.: The Effect of Unilateral Spontaneous Pneumothorax on the Circulation in Man. J. Clin. Investigation **19**: 321, 1940.

Certain studies were made of the circulation of four patients exhibiting unilateral spontaneous pneumothorax of unknown etiology. None of the patients showed either demonstrable pulmonary pathology or organic heart disease. Studies were made at various levels of collapse and after complete expansion.

The cardiac output appeared to be reduced in the presence of unilateral pneumothorax of small or moderate size, although it was sometimes unchanged or even increased. Patients exhibiting more extensive pneumothorax showed a reduction in cardiac output which might be large or small. When the data for all cases were pooled, a rough linear correlation appeared between both cardiac output per minute and per beat, and per cent collapse of the lung, since the greatest collapse was associated with the greatest decrease in cardiac output; as the amount of collapse decreased, the cardiac output increased. In one of our patients who was observed during collapse of only 14 per cent, there was an increase in cardiac output. This finding is similar to one made by Hilton in goats, namely, that a small collapse gives rise to an increase in volume output of blood from the heart.

The decrease in vital capacity bears a linear relation to the per cent collapse of the lung.

Since unilateral collapse of a lung usually results in decrease in the volume of blood expelled by the heart per minute, the institution of this procedure should be considered carefully before it is undertaken in subjects suffering from lesions which may themselves be associated also with decrease in output. This precaution is necessary in order to avoid an accumulated reduction in cardiac output.

AUTHORS.

Johnston, Franklin D., and Kline, Edward M.: An Acoustical Study of the Stethoscope. Arch. Int. Med. **65**: 328, 1940.

A method is described for testing stethoscopes in an acoustic system similar to the one that is present during auscultation in the clinic.

The results with this method indicate that:

The bell with a shallow chamber is superior to other end pieces of the bell type.

A rubber nipple placed over the terminal portion of a bell improves its performance.

The diaphragm of a Bowles end piece acts as a filter to suppress the transmission low-pitched sounds, but the diaphragm must be stiff to be effective in this respect.

Although rubber tubings of different lengths, diameters and degrees of stiffness modify transmission, largely because of resonance phenomena, the differences are relatively small, and the response of a stethoscope depends more on the choice of the end piece than on the nature of the tubes that are used.

AUTHORS.

Starr, Isaac, and Rawson, Arthur J.: Role of the "Static Blood Pressure" in Abnormal Increments of Venous Pressure, Epecially in Heart Failure. (1. Theoretical Studies on an Improved Circulation Schema Whose Pumps Obey Starling's Law of the Heart.) Am. J. M. Sc. **199**: 27, 1940.

A circulation schema is described whose pumps obey Starling's Law of the Heart.

On this schema the static blood pressure, i.e., the pressure existing at all points in the circulation when the "heart" is stopped, is an important factor in compensation for weakness of the "heart" and in the causation of increased "venous" pressure.

The arterial and venous pressures of clinical congestive failure cannot be reproduced in this schema by weakening the heart alone. Mechanisms which cause an increase of static blood pressure, such as general vasoconstriction, pressure on vessels from without, or the insertion of additional fluid within the vessels, must be introduced before the pressure relations of clinical congestive heart failure can be produced.

The behavior of the schema has suggested clinical considerations which raised doubt whether the venous congestion of "congestive heart failure" was brought about in the manner commonly believed. This prompted the clinical investigations reported in the following paper.

AUTHORS.

Starr, Isaac: Role of the "Static Blood Pressure" in Abnormal Increments of Venous Pressure, Especially in Heart Failure. II. Clinical and Experimental Studies. Am. J. M. Sc. **199**: 40, 1940.

The pressure remaining throughout the circulation after the cessation of cardiac action, the "static blood pressure," has been measured promptly after death in sixty-four patients. Necropsies were performed in forty-four of these cases.

In persons dying of prolonged congestive heart failure the static blood pressure averaged 20.3 cm. H_2O. In persons dying without heart disease it averaged 7.6 cm. This difference is large enough to account for the major part, in some instances for all, of the high venous pressure found in cases of congestive failure during life.

Obviously, therefore, the larger part of the increase of venous pressure found in cases of congestive failure should not be attributed directly to any difference of cardiac function, for the abnormality persists when the heart is no longer functioning.

Well-known theoretical conceptions in congestive failure have been restudied and reassessed in the light of this new information.

AUTHOR.

Freundlich, J., and Lepeschkin, E.: Systemic Studies of Chest Leads in Left and Right Axis Deviation Types of Electrocardiograms. Cardiologia **3**: 331, 1939.

Eighty cases with left and twenty-seven with right axis deviation were studied; none had myocardial infarction or prolonged QRS. Sixteen chest points were used, and the "indifferent" electrode was on the left leg.

In the left axis deviation with upright T_1, the chest leads resembled the normal. However, when T_1 was inverted, the QRS was upright and the T wave was inverted in the right anterior chest surface, and QRS was inverted and T was upright on the left side; the transition between these two areas was abrupt. This configuration occurred with enlarged left ventricle and old or recent heart failure. When T_1 is isoelectric the chest leads of left axis deviation were intermediate.

Right axis deviation also showed two types of chest leads. In one type QRS was inverted over the entire anterior chest, with T inverted or isoelectric except in the left anterior axillary line. In the second type, QRS on the right side of the chest was mainly up with T inverted, and on the left side it was mainly down with the T wave up.

KATZ.

Lüderitz, B.: The Relation Between QRS Duration and the Form of S-T Segment in the Human Electrocardiogram. Arch. f. Kreislaufforsch. **5**: 223, 1939.

Five hundred normal electrocardiograms were analyzed. The duration of QRS was found to vary between 0.06 to 0.12 second with a typical distribution curve

and a mean of 0.08 second. The author concludes that a QRS less than 0.08 is normal; 0.09 to 0.10 may be normal; over 0.10 is usually evidence of prolonged intraventricular conduction. Two hundred and eighty-seven other electrocardiograms were analyzed in which S-T in Lead I or II or in both was depressed and these compared with normals. It was found that while the scatter was toward the longer duration of QRS, practically all QRS durations fell in the normal range.

KATZ.

Herve, L. Luis, and Santander, Manuel Besoain: The Electrocardiogram in Exercise. Rev. argent. de cardiol. **6**: 299, 1939.

The alterations of the electrocardiogram caused by exercise were investigated in thirty normal subjects of different ages. Small variations in the amplitude of the waves and in the duration of intervals between them were found as well as depression of the S-T interval of even more than 2 mm. in some cases.

In cardiac patients pathologic alterations appear after exercise in 27 per cent of the cases which had normal electrocardiograms at rest; this proportion is even higher (35 per cent) if only those patients with coronary disease are considered. The alterations induced by exercise and considered indicating myocardial disease of coronary origin are: inversion of the T wave in any of the leads in which it was positive, appearance of arrhythmia or auriculoventricular or intraventricular block, and prolongation of the Q-T interval.

The depression of the S-T interval induced by exercise has a very restricted value as a sign of coronary insufficiency.

AUTHORS.

Bang, Ole: Gonorrhoeal Myocarditis. Brit. M. J. **1**: 117, 1940.

Apart from the myocardial involvement in the bacterial endocarditis of gonococcal septicemia, myocarditis is seldom established as a complication in gonococcal infection. In view of this it seems surprising that a series of six instances of what is regarded as gonorrheal myocarditis was encountered in the course of one year in an ordinary medical ward. It seems probable that this condition often escapes detection, since suggestive symptoms may be absent.

The diagnosis was made on the ground that all six cases had changes in the electrocardiogram occurring in the course of acute or chronic complicated gonococcal infection. In some instances the myocarditis was slight and transitory, as may be the case in many simple infections, for example, pneumonia. However, in two cases incomplete bundle branch block developed and persisted, and in a third case the anginal pain still troubled the patient considerably when he was reexamined a year later. Such a course suggests the possibility that some of these patients will return to hospital sooner or later with chronic heart disease. It is possible, also, that some of the chronic "degenerative" heart diseases which we see today arise from gonococcal infection.

The gonococcal complement-fixation reaction has been instrumental in pointing out how great a proportion of so-called rheumatic arthritis cases were really gonorrheal. It may be worth while to search the anamnesis of heart patients for gonorrhea as we search it for syphilis and rheumatic fever, and the complement-fixation reaction may reveal that some instances of heart lesion attributed to rheumatic infection ought to be regarded as following on persistent gonococcal infection.

AUTHOR.

Noth, Paul H., and Barnes, Arlie R.: Electrocardiographic Changes Associated With Pericarditis. Arch. Int. Med. 65: 291, 1940.

In acute pericarditis the most characteristic electrocardiographic change consists in elevation of the RS-T segment and in exaggerated T waves in the standard leads. The RS-T segment may be elevated in all three leads, which constitutes the most characteristic picture, or in Leads I and II, in Leads II and III, or in Lead I alone. Reciprocal depression RS-T_3 when RS-T_1 is elevated and depression of RS-T_1 when RS-T_3 is elevated are rarely observed, and this characteristic serves to distinguish these changes from those observed after acute myocardial infarction. In acute pericarditis the ascending limb of the elevated RS-T segment is concave or ascends as a straight line of an upward inclined plane, in contrast to the convex contour of this limb seen frequently in tracings in cases of acute myocardial infarction. In the early stage the T wave may be exaggerated and rather sharp, or they may have a dome-shaped summit.

The elevation of the RS-T segment in acute pericarditis is apt to be transitory, certainly more so on the average than the elevation observed after acute myocardial infarction. In the subacute stage of pericarditis the elevations disappear and the standard leads may return to normal or be followed by T waves of low voltage, by dome-shaped or isoelectric T waves, or by actual negativity of the T waves. Negativity or low voltage of the T waves in all the standard leads constitutes the most suggestive picture of pericarditis at this stage. The T wave, if inverted, may have a contour closely resembling the "cove plane" T wave observed in the stage of healing of myocardial infarction, though frequently it lacks the depth of the T wave commonly observed in the latter condition.

Elevation of the RS-T wave segments and exaggerated T waves in the standard leads can be produced by a rapidly accumulating effusion, but effusion is not essential in the production of such changes.

The presence of pericarditis complicating coronary occlusion will be signalized chiefly by elevation of the RS-T segments in the three standard leads or in Leads I and II, with little or no elevation but with absence of reciprocal depression of the segment in Lead III. If this pattern is succeeded by negativity of the T waves in all the standard leads, the evidence for pericarditis complicating coronary occlusion is greatly strengthened. It is probable that pericarditis complicating acute infarction of the posterior portion of the left ventricle will cause elevation of RT_1 or prevent the depression of ST_1, normally anticipated in this condition. Pericarditis complicating acute myocardial infarction frequently interferes with the development of T_1 and T_2 patterns. However, Q_1 and Q_3 patterns may be present to indicate the site of infarction and to suggest that pericarditis alone is not responsible for the electrocardiographic changes. Absence of a Q wave in the Wolferth lead and of an R wave in Lead IV suggests, but does not denote positively, that acute infarction of the anterior portion of the left ventricle has occurred.

In tuberculous pericarditis we have not observed the elevation of the RS-T segment, though it is conceivable that it might occur in an acute stage. The changes observed in this condition are chiefly those observed in chronic constrictive pericarditis and at certain stages of healing in acute pericarditis in some patients include (1) low voltage of the QRS complexes in all the standard leads, (2) low voltage of the T waves in all standard leads, or, in most characteristic instances, inversion of the T waves in all standard leads, and (3) dome-shaped, flattened, isoelectric or negative T waves in one or more standard leads.

Typical Q_1 or Q_3 patterns have not occurred in our series of cases of pericarditis unassociated with acute myocardial infarction.

The precordial lead may or may not exhibit significant changes. The chief changes observed are reversal of the normal direction of or shallowness of the T

wave. In acute pericarditis there is a tendency to depression of the RT segment in the Wolferth lead, though it may be absent when elevations of the RS-T segment are present in the standard leads. In most instances the Q wave is preserved in a normal form, an observation which is of considerable value in excluding the occurrence of acute infarction of the anterior portion of the left ventricle.

Unless tracings are taken within two or three days after the onset of acute pericarditis, diagnostic electrocardiographic changes may be missed. Serial tracings taken over a period of days, or even weeks, may be required to differentiate the tracings of pericarditis from those of acute myocardial infarction. A rapid return to normal is often sufficient to exclude the latter condition.

Considerable experience and detailed knowledge may be required to recognize the electrocardiographic evidence of pericarditis. Occasionally the signs are diagnostic. Frequently they are suggestive and direct clinical studies toward the proper diagnosis. They must be correlated with the clinical picture and observations to serve their greatest usefulness. Familiarity with the changes is essential if confusion with other cardiac lesions is to be avoided. Pericarditis is much more frequent than is suspected; its recognition is often difficult but highly important, and a proper understanding of the electrocardiographic changes produced by it will result in a great increase in the proportion of cases recognized in medical diagnosis.

AUTHORS.

Nelson, Arthur A.: Pericardial Milk Spots. Arch. Path. **29**: 256, 1940.

Pericardial milk spots occurred in 170 (34.4 per cent) of 494 persons 1 year or more of age. In 439 persons 18 or more years of age the incidence was 37.6 per cent. In general, there is an increase of incidence with age, but this increase is by no means rectilinear. The spots are scarce in children and very frequent in old age, but between 35 and 75 years of age there is little change in incidence.

There seems to be a definite association with chronic or recurrent valvular heart disease; of forty-two persons with such disease, twenty-eight (66.7 per cent) showed spots. Patients with severe coronary sclerosis and enlarged hearts showed fairly definite increases (50.0 and 47.9 per cent, respectively).

The occurrence of more than one spot is slightly more frequent than that of only one. Spots occur on the right side, anteriorly, and on the ventricles much more frequently than they do on the opposite surfaces.

Old pleural adhesions are slightly more frequent in patients with spots than in those without.

Fifteen or 20 per cent of spots show appearances (projecting villi, cellular exudation, subepithelial palisading or epithelial enclosures in collaginous tissue) which suggest transitions from a more active inflammatory process to the usual type of milk spot.

AUTHOR.

Epstein, Bernard S.: Comparative Study of Valvular Calcifications in Rheumatic and in Nonrheumatic Heart Disease. Arch. Int. Med. **65**: 279, 1940.

Slight and moderate calcifications in the mitral valves of patients with rheumatic heart disease occurred most frequently in the leaflets. The free margins were often involved when the lesions were extensive. The smallest deposits were situated on the bodies of the leaflets or the endocardium of the left auricle adjacent to the insertion of the leaflets. Advanced valvular deformity was associated with the calcifications in almost every instance, regardless of the degree of calcification.

Calcifications of the aortic valve in patients with rheumatic heart disease who were under 30 years of age were accompanied in each instance by extensive changes and calcifications in the mitral valve. In two persons the tricuspid valve was involved also.

The incidence of calcifications of the aortic valve rose sharply after the age of 40. The lesions of the aortic valve associated with the calcific deposits in older patients were usually less extensive than those in younger persons. Frequent association with lesions of the mitral valve was noted, but calcifications in the mitral leaflets in such persons were not common.

In patients with nonrheumatic heart disease calcifications of the mitral valve involved the annulus. Concomitant valvular defects were uncommon in this group. It is noteworthy that the auscultatory findings were within normal limits. This may indicate that the calcifications did not produce significant changes either in the anatomic function of the valve or in the heart sounds.

Calcifications of the aortic valve in nonrheumatic heart disease were equally frequent in the leaflets and in the annulus. In some instances both structures were involved. Aortic valvular defects due to calcific deposits were relatively frequent, but as a rule were not as extensive as those seen in cases of rheumatic heart disease with calcification of the valves. However, advanced calcifications of the aortic valve were present in patients who had had neither clinically demonstrable defects of the aortic valve nor symptoms of heart failure. The weights of the hearts with calcified valves were independent of the presence of calcifications. Disease of the coronary arteries and aortic arteriosclerosis with calcification were more frequent in the nonrheumatic than in the rheumatic group. Nevertheless, patients with rheumatic heart disease who had survived the age of 40 had calcific deposits similar in extent and distribution to those patients with nonrheumatic heart disease. The incidence of calcifications of the aortic valve was definitely greater in the rheumatic group after the age of 40. It is reasonable to assume that the same process might be responsible for the calcifications in the two groups. The possibility of calcification occurring on the site of an old rheumatic lesion, thereby speeding the disease process, has been mentioned.

Pericarditis was more frequent in the rheumatic group, and may when present provide a clue pointing to a rheumatic origin.

From the clinical viewpoint, the presence of calcifications in the heart valves did not appreciably alter the prognosis. Nor did there seem to be any relationship between the duration of symptoms of heart failure or of known heart disease and the presence of calcareous deposits. The symptoms of heart failure appeared to be related to the effect of the valvular deformity on the myocardium, and the degree of deformity apparently may be the same with or without calcareous deposits. This is borne out by the similarity in the incidence of heart failure in patients with rheumatic heart disease and in those without valvular calcifications as well as by the relatively low incidence of heart failure in the group with non-rheumatic heart disease with valvular calcifications.

The lack of influence of calcifications in the valve on the heart sounds may best be represented by the absence of significant auscultatory changes in the patients with nonrheumatic heart disease associated with a calcified mitral annulus.

AUTHOR.

Walsh, Bernard J., Bland, Edward F., and Jones, T. Duckett: Pure Mitral Stenosis in Young Persons. Arch. Int. Med. **65**: 321, 1940.

From a clinical study of eighty-one young patients who have acquired the physical signs of so-called pure mitral stenosis it has been shown that:

The evolution of the physical signs prior to the establishment of this deformity required in the majority from five to fifteen years.

A relatively mild form of rheumatic fever appears to favor the development of this particular lesion.

The prolonged course of the disease in most patients with this deformity is fundamentally dependent on a benign type of rheumatic fever.

AUTHORS.

Gauld, Ross L., and Read, Frances E. M.: Studies of Rheumatic Disease. III. Familial Association and Aggregation in Rheumatic Disease. J. Clin. Investigation **19**: 393, 1940.

The children of ninety-five families, in each of which one child entered the clinic because of some rheumatic manifestation, were studied with respect to the relationship to the occurrence of the disease among them to familial association with an acute episode of the disease in another member of the family. As far as possible hereditary factors were held constant throughout the analysis, and the index cases were excluded from the tabulations because of the bias which they introduced.

The analysis showed that the risk of contracting the disease among the siblings of the index cases was increased, following association with an acute episode of the disease in another member of the family, to more than twice that which prevailed prior to this association. This suggests that there is an environmental factor which plays a role in the causation of this disease.

The children of rheumatic parents had higher attack rates than the children of nonrheumatic parents, both before and after their first familial association with an acute episode. The interpretation of this finding should be made with caution because the children who have parents with a rheumatic history are, in most instances, also associated with what might be called the chronic quiescent phase of the disease in these parents. The higher incidence in these children could, therefore, be due to either to an increased hereditary susceptibility or to long continued association with the disease in chronic form. Considered along with the findings of the previous article, the first would seem to be more probable explanation, i.e., that heredity plays a definite role in the etiology of the disease.

The time relation between episodes in the family and the occurrence of subsequent cases in other members did not show a definite tendency for the incidence of subsequent attacks to be highest within short time intervals of an association with acute episodes. This finding would suggest that either long continued exposure to the cause (whether it be parasitic or nonparasitic) is necessary, or that the disease is slow in developing to the point where it becomes clinically manifest. In this respect, if it be due to an infection, it therefore resembles tuberculosis rather than an acute infection such as scarlet fever or diphtheria, and the results of exposure in any household should not be measured in weeks or months, but in years.

These findings are consistent with the hypothesis that in the etiology of rheumatic disease there are both hereditary and environmental factors involved and that the environmental factors to produce the disease must act over a long period of time, and/or the disease has a long period of subclinical development before becoming manifest. They are consistent with such hypothesis, but do not prove it, because other explanations could fit the observed facts.

AUTHORS.

Wilens, Sigmund L.: Relation of the Elastic Tissue in the Root of the Aorta to the Aortic Valve: Involvement of this Tissue in Syphilis. Arch. Path. **29**: 200, 1940.

Measurements on the nonsyphilitic aorta reveal that the elastic tissue of the media at the root may project a variable distance proximal to the commissural

attachments of the aortic valve cusps and that the lateral attachments of the cusps may show a great deal or very little of the medial coat in the wall of the underlying aorta. These variations do not appear to be related to the size of the aorta or heart and are not influenced by age, sex, body length, or heart weight.

Since the lateral attachments of the aortic cusps are chiefly involved in the development of aortic insufficiency due to syphilis, it is pointed out that the degree of valvular damage may depend in part on the extension of the media in this area.

Measurements on the syphilitic aorta support this concept. The elastic tissue of the media is found to end more abruptly at the commissures in cases in which aortic insufficiency has failed to develop than in cases in which the valves are incompetent.

The three commissures in the normal aorta have different amounts of elastic tissue in their walls. Although the relative degree of involvement of each of the three commissures varies in individual cases, in a series of cases of syphilitic aortitis with aortic insufficiency the average degree of involvement varied directly with the amount of intramural elastic tissue.

The highest point of attachment of the aortic cusps is found to be lower in the syphilitic aorta than in the normal one. This displacement is not related to changes in the leaflets themselves, since it is found when the cusps are still delicate and normally inserted.

AUTHOR.

Hochrein, M., and Dinischiotu, G. T.: The Pathogenesis of Bronchial Asthma. Ztschr. f. Kreislaufforsch. **31**: 465, 1939.

Vagus stimulation in certain instances (two cases in which doryl was used) can cause bronchial asthma. The pattern of respiration in such cases, during the attack and in intervals between attacks, was analyzed and evidence in the contour was found reminiscent of the breathing pattern in pulmonary stasis. The effect of obstruction of air passages in animals was investigated and it was found that this caused accumulation of blood in the lung and a decrease of that held by the spleen. This mechanism is believed to operate also clinically. The authors conclude, therefore, that in bronchial asthma there is a similar circulatory disturbance. In 200 cases it was found that 24.5 per cent had chronic bronchitis, 13 per cent had emphysema, 11.5 per cent had "anaphylactic" phenomena like eczema, 9 per cent had pneumonia, 9 per cent had tuberculosis, 6 per cent had psychoses, 5.5 per cent had metabolic disorders, etc.

KATZ.

Naumann, M.: The Blood Pressure in the Dorsal Artery of the Foot Under Normal Conditions and in Circulatory Disturbances. Ztschr. f. Kreislaufforsch. **31**: 513, 1939.

In twenty-six out of 145 patients apparently free of circulatory disorders, it was found that the pressure in the dorsalis pedis was lower than in the radial artery. In the rest the reverse was true.

KATZ.

Tellenbach, H.: Pleural Transudation as a Sign of Right Heart Insufficiency. Ztschr. f. Kreislaufforsch. **31**: 771, 1939.

Two cases are presented and correlated with the literature. It was found that congestion behind the right heart will slow the circulation in the pleura and thus lead to transudation. This may be aided by retardation of lymphatic flow into the congested systemic veins.

KATZ.

Pines, Ignacy: Experimental Studies of Air Embolism. Cardiologia 3: 308, 1939.

Air was injected into the jugular vein or left auricle of the cat. Venous air caused foaming of blood which passed into the right ventricle and pulmonary artery and its branches. Death ensued if the pulmonary circuit was completely obstructed, otherwise there was only a temporary drop in aortic pressure. Some of the air passed into the left heart and systemic circuit. Some was absorbed by the blood, some passed out into the alveoli.

Air entrance into the left ventricle may have serious effects because coronary embolism may occur, but this is rare. In the cat air in the amount of twice the amount of the heart stroke volume could be injected without a fatal result. In the dog ventricular fibrillation was more readily produced.

KATZ.

Young, R. A.: The Pulmonary Circulation, Before and After Harvey. Brit. Med. J. 1: 1 and 41, 1940.

This is the annual Harveyian oration delivered before the Royal College of Physicians in London. It is a complete review of present knowledge of the pulmonary circulation. The historical review is complete, and there is an accurate description of the part played by the pulmonary circulation in physiology and disease of the cardiovascular system.

MCCULLOCH.

Robinson, Roger W., and O'Hare, James P.: Further Experience With Potassium Sulfocyanate Therapy in Hypertension. New Eng. J. Med. 221: 964, 1939.

Seventy-five patients with hypertension were treated with potassium sulfocyanate given by mouth. All were ambulatory. All were followed closely by blood-cyanate studies. Maximum drops in blood pressure of over 100 mm. systolic and 35 mm. diastolic were observed in three cases. Average drops of 40 mm. systolic and 20 mm. diastolic occurred in 63 per cent of the patients. Symptomatic effects of the drug were noted chiefly in the relief of hypertensive headaches in eighteen out of twenty cases. Toxic symptoms occurred in twenty-nine cases or 38 per cent. The less serious complications, accounting for twenty-three of these twenty-nine cases, consisted of nausea, weakness, dermatitis, purpura, and a decrease in libido. Serious complications consisting of dermatitis exfoliativa, congestive heart failure, cerebral thrombosis, angina pectoris, and psychoses occurred in six cases. From our experience with sulfocyanate therapy, we have concluded that this form of treatment of uncomplicated vascular hypertension in patients under 60 years of age, when carefully controlled, has decided value.

AUTHORS.

deTakats, Géza: Analysis of Results Following Sympathectomy for Peripheral Vascular Disease. Am. J. Surg. 47: 78, 1940.

The indications for sympathectomy in peripheral vascular diseases are discussed. The effect of sympathectomy is to prevent the great fluctuations in blood flow which are produced by various vasoconstrictor stimuli, such as cold, pain, fright, or anger. The analysis of the results indicates that sympathectomy has a definite place in the treatment of peripheral circulatory disturbances.

NAIDE.

Hilbing, R.: Simultaneous Electrocardiogram and Histological Observations of Digitalis Poisoned Cat Hearts. Arch. f. Kreislaufforsch. 5: 292, 1939.

Digitalis excess, as others have found, caused typical S-T and T changes and, in some, reversal and widening of QRS. In most animals, disseminated focal necrosis was found in the ventricular muscle and in the auricular wall. These were particularly prominent in the left ventricle. In most animals alterations in the large branches of the left bundle were also seen.

KATZ.

Wagenfeld, E.: The Action of Strophanthin in Irregular Heart Action. Arch. f. Kreislaufforsch. 5: 310, 1939.

In this report forty-nine cases of disturbances of impulse conduction and initiation of some duration were studied. The etiology of the majority was varying combinations of coronary sclerosis with or without angina pectoris or myocardial infarction and hypertension or lues; a few were of an infectious origin. Analysis showed that fundamentally the arrhythmias developed because of a disparity between the mass of the heart and the coronary blood supply. The author attributes the appearance of extrasystoles, paroxysmal tachycardia, auricular fibrillation, and conduction disturbances during strophanthin therapy to coincidental alterations in coronary flow rather than to an effect of the drug itself. As the cardiac failure is improved with strophanthin, the irregularities disappear. In short, this study supports the contention of Edens (1) that strophanthin can lead to the relief of these arrhythmias when they are evidence of heart failure and (2) that their occurrence during medication is not always attributable to the action of the drug or aggravation by it, but to the occurrence of coronary insufficiency.

For details, this monograph of 100 pages (with extensive bibliography) should be consulted.

KATZ.

Osterwald, K. H., and Meurer, H.: The Effect of Strophanthin on the Blood Vessels and Its Role in Determining Minute Volume Flow. Ztschr. f. Kreislaufforsch. 31: 522, 1939.

Twenty anesthetized dogs were used. The blood pressure and blood flow were measured, the latter with the Rein stromuhr, after intravenous strophanthin in therapeutic doses. The flow was measured in the kidney, intestinal tract extremity, or in the inferior vena cava.

The authors conclude from their studies that the decreased cardiac output is caused primarily by a decrease in flow through the splanchnic and extremity vessels, and only later by a decrease in flow through the liver sluiceway mechanism.

KATZ.

Osterwald, K. H., and Meurer, H.: The Effect of Diethylanolamine, Ethyldiamine and Isopropanolamine on the Action of Theophyllin on the Coronary Vessels and General Circulation. Ztschr. f. Kreislaufforsch. 31: 593, 1939.

Diethylanolamine only has a beneficial effect on the heart on coronary flow. Ethyldiamine causes a decrease in cardiac minute volume output and in coronary flow. Isopropanolamine causes a primary slowing and a secondary increase in coronary flow. These studies were carried out on twenty anesthetized dogs, using the Rein stromuhr for coronary and inferior vena cava or pulmonary flow measurements.

KATZ.

Roemheld, L.: Effect of Low Calory Diet on the Minute Volume of the Heart of Man. Ztschr. f. Kreislaufforsch. **31**: 668, 1939.

A comparison is made of the effect of high and low calory diet on ten patients. A decrease of one-fourth liter minute was found on the average on the low calory diet.

KATZ.

Nordenfeldt, O.: Electrocardiographic Change Caused by Orthostatic Circulatory Disturbances and Ergotamine Nitrate. Ztschr. f. Kreislaufforsch. **31**: 761, 1939.

Electrocardiographs were taken in the upright and recumbent position, in twenty normal subjects and in three with orthostatic circulatory disturbances before and after 0.5 mg. ergotamine tartrate was injected intravenously. It was found that the ergotamine caused the disappearance of the electrocardiographic changes noted in the upright position before the injection of the drug. This is believed to indicate that the electrocardiographic changes are due to increased sympathetic nerve action on the heart.

KATZ.

Hartleb, H. O.: Folinerin and the Electrocardiogram. Ztschr. f. Kreislaufforsch. **31**: 801, 1939.

Folinerin, alpha oleander glucoside, has a digitalis effect on the electrocardiogram. This appears in two to three days and disappears just as rapidly after medication is stopped. It has other digitalis effects. Twenty to thirty drops were used three times a day, and rarely as much as forty drops were used. Maintenance doses can be continued for long periods. Ten cases are reported.

KATZ.

Kisch, F.: Functional Criteria for the Use of Cardiac Therapy in Extreme Obesity. Cardiologia **3**: 219, 1939.

Increased dyspnea in an extremely obese person on assuming the recumbent position is a sign of cardiac insufficiency whereas alleviation of dyspnea in the recumbent position is due to the action of excessive intra-abdominal fat hampering diaphragmatic activity in the upright position. Oliguria which responds only once to mercurial diuretics is not apt to be caused by heart failure.

KATZ.

Book Reviews

ELECTROCARDIOGRAPHIC PATTERNS: By Arlie R. Barnes, M.D., the Mayo Clinic, Rochester, Minn. 195 pages, 94 figures. Price, $5.00. Springfield, 1940, Charles C. Thomas.

During the past twenty-five years, the clinical applications of electrocardiography have assumed increasing importance. First used to elucidate the nature of the disturbed mechanism in the arrhythmias, the method has been employed intensively in the study of diseases of the coronary arteries and myocardial infarction. It has been helpful also in the recognition and management of various other disorders of the heart.

In this compact volume, the author, after assembling a mass of material, has digested it and made certain groupings which he has called "patterns." He states clearly in his introduction that, although not uncommonly such patterns may be of crucial diagnostic value, more frequently they serve to corroborate a clinical impression. "Their usefulness will not therefore supplant clinical acumen, but rather will depend on sound clinical judgment." The scope of the discussions is shown by the following chapter headings: The Relation of the Distribution of the Coronary Arteries to Acute Myocardial Infarction; The Electrocardiogram in Acute Myocardial Infarction and in Its Healing Stages; The Electrocardiogram in Predominant Ventricular Strain; The Electrocardiogram in Acute Right Ventricular Strain (Acute Cor Pulmonale); The Electrocardiogram in Chronic Right Ventricular Strain; The Electrocardiogram in Pericarditis; The Effects of Certain Drugs, Metabolic Disorders and Infections on the Electrocardiogram; Some Observations Relative to Precordial Leads.

The sections on myocardial infarction and pericarditis are particularly good. The importance of ventricular strain, a subject in which the author and his colleagues have been especially interested, has perhaps been unduly stressed. The tables of measurements of standard and precordial leads in 100 normal persons contain valuable data. The figures are numerous and clear. Some of the descriptive legends, it seemed to the reviewer, would be more effective if they were more concise. There is an excellent bibliography. It is regrettable that most of the precordial leads were taken before standards were established by the American Heart Association, for, according to these standards, in almost all of the tracings the waves in the chest leads are reversed.

The book is not a text for beginners. Rather should it be regarded as a reference monograph for those who have had some experience in interpreting electrocardiograms. The author has performed a real service in bringing together scattered contributions, including many of his own, which have appeared in the literature. By selecting and arranging them in critical fashion, he has made them readily available and has crystallized current concepts.

ROBERT L. LEVY.

HIPERTENSION ARTERIAL NEFRÓGENA; ESTUDIO EXPERIMENTAL: By Dr. Juan Carlos Fasciolo, Institute of Physiology (Prof. Houssay). Buenos Aires, 1939, 155 pages, 42 illustrations.

Chapter I deals with the methods for the measurement of arterial pressure in dogs. Chapter II deals with the Goldblatt method of producing incomplete

renal ischemia and hypertension. Chapter III deals with the nervous system in relation to experimental hypertension. The author concludes that (1) denervation of the kidney does not prevent the development of hypertension, (2) section of the splanchnic nerves, with excision of the last dorsal ganglion, does not prevent the development of experimental hypertension, and (3) sympathectomy does not prevent the development of experimental hypertension. Chapter IV deals with original work by the author. An incompletely ischemic kidney was transplanted to the vessels of the neck in a dog. Both kidneys were removed from the dog two hours before transplantation. In twenty-two of twenty-four experiments of this type the increase in arterial pressure ranged from 20 to 70 mm. of mercury. In twenty-five control experiments in which a normal kidney was transplanted there was no rise in twenty-two and a rise of 45 to 70 mm. in three. The author believes that the cause of the hypertension is a substance produced by the partially ischemic kidney. Chapter V considers the action of the venous blood from an incompletely ischemic kidney on the circulation of the frog. The studies show (1) that the venous blood from the ischemic kidney, with few exceptions, has a marked vasoconstrictive action on the vascular system of the frog, (2) that venous blood from other organs of the renal hypertensive dog has this vasoconstrictive action, but to a lesser degree, (3) that the venous blood of the uremic dog possesses no vasoconstrictive action, (4) that the ultrafiltrate of the citrated plasma of the venous blood from the ischemic kidney of the hypertensive dog does not produce vasoconstriction, and (5) that the normal kidney of a dog with unilateral renal ischemia and hypertension destroys or eliminates the pressor substance of the ischemic kidney. Chapter VII discusses the role of the endocrine glands in the hypertension produced by renal ischemia. On the basis of this research, the author concludes that grafting an ischemic kidney to a bilaterally nephrectomized dog which has had both suprarenals removed produces as much of an increase in arterial pressure as it does when the adrenals have not been removed. The remainder of the book takes up lesions of the eyes, and the anatomic lesions of the kidney, bladder, intestines, pancreas, stomach, and heart. The surgical treatment of hypertension in man is considered. The book is a good presentation of the subject, and includes the experimental work of the author.

ARNALDO YODICE AND CLAUDE S. BECK.

STUDIEN ÜBER DAS VERHALTEN DES VENENDRUCKES BEIM VALSALVASCHEN VERSUCH: By Knut Liedholm, Medizinische Universitätsklinik zu Lund. 1939, Håkan Ohlssons Buchdruckerei, 213 pages, 50 illustrations.

This monograph describes a very careful study conducted on groups of normal persons, patients with hypertension, and patients with valvular heart disease. The results are of greater physiologic than clinical interest. There is a good summary in English.

ISAAC STARR.

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